DEVELOPING AN AMISH AND MENNONITE RESEARCH REGISTRY IN WESTERN PENNSYLVANIA

by

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ABSTRACT

The Amish and Mennonites of western Pennsylvania are genetically isolated religious communities that are disproportionally burdened by genetic disease due to founder and bottleneck effects from their European migration in the 17th century. Research studies to better understand the types of conditions in the communities, the natural history of these conditions, as well as health care needs of these communities, will allow for more targeted delivery of appropriate healthcare interventions. However, barriers exist for identifying and ascertaining appropriate members of the Plain Community for research studies. The Plain Community is considered a vulnerable population because of their unique cultural identity, relative isolation, and limited utilization of mainstream to healthcare. Vulnerable groups are often difficult to reach, however, there has been support for community based research registries as a way to address disparities for access to and participation in research. An Amish and Mennonite Research Registry was developed in western Pennsylvania to diminish these barriers and provide a platform for contacting willing members of the Plain Community for participation in future research projects that may positively impact future medical care, as well as the general care in their communities. Improving working relationships among Amish, Mennonites, and researchers has public health significance because it could improve health care delivery to the Plain

Communities in western Pennsylvania. We developed a culturally appropriate approach for recruiting and consenting members of this vulnerable population. This paper reports on the development and implementation process of the research registry and its public health importance.

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PREFACE

This project was made possible by the efforts of many supportive individuals who I would like to take the opportunity to formally thank. First, thank you to the Medical Genetics Division at Children's Hospital of Pittsburgh of UPMC for providing me with the resources to carry out this project. Secondly, I am extremely appreciative of my thesis advisor, Catherine Walsh Vockley, for helping me develop this project and for the guidance throughout the process. I would also like to thank my thesis committee members, Dr. Ghaloul Gonalez, Dr. Durst and Dr. Grubs, for your support and feedback. Lastly, I would like to thank my family and friends for the continued support along this graduate school journey.

1.0 INTRODUCTION

The Amish and Mennonite communities of western Pennsylvania are unique because they are isolated both geographically and socially. These groups are descendants of the 16th century Anabaptists living in Europe during a time of Christian church reform.[1–4] Due to the persecution that the Amish and Mennonites faced in Europe, many groups fled, accepting an offer of religious freedom from William Penn, settling in what is now known as Pennsylvania[1–4]. Since this first settlement, there have been additional migration events within North America that have resulted in several distinct communities.[2,4,5] These events lead to genetic founder effects, genetic bottleneck effects and virtually zero genetic inflow, due to cultural preferences to marry within the community.[2] The result has been an increased burden of specific genetic disease in these communities.[2,3] Specific founder gene mutations explain the prevalence of different genetic conditions within each community and family group.[2,3] This means that families and communities will have a clustering of certain genetic conditions, while the prevalence among the Plain People as a whole remains low.[2,3] Understanding the specific needs of each family and community group is important in order to deliver comprehensive and specialized care.

Research studies to better understand the types of conditions in the communities, the natural history of these conditions, as well as health care needs of these communities, will allow for more targeted delivery of appropriate healthcare interventions. Currently, in eastern Pennsylvania, the Clinic for Special Children in Strasburg is providing primary care medicine

and conducting research to improve access and quality of care for Plain Communities. There is a need for a similar understanding and relationship with the Plain Communities of western Pennsylvania.

Challenges exist for identifying and ascertaining appropriate individuals within the Plain Community for new research studies. This is largely due to their social and geographical isolation related to religious and cultural practices. Improving research and understanding of Plain Communities has the potential to improve early diagnosis, interventions, and clinical outcomes. Creating an ongoing research registry will break down barriers and provide a platform for contacting willing members of the Plain Community for participation in future research projects that may positively impact medical care, as well as the general care in their communities. This project focuses on the development and implementation of an Amish and Mennonite Research Registry in western Pennsylvania.

1.1 SPECIFIC AIMS

Aim 1: To identify and ascertain members of the western Pennsylvania and eastern Ohio Plain Communities. To devise a culturally appropriate approach for contacting and consenting, which includes the development of a brochure.

Aim 2: To construct a detailed extended family pedigree for each consented participant and to collect a detailed medical history.

Aim 3: To create a registry for identifying and contacting appropriate members of the Plain Communities for participation in future research studies.

Aim 4: To report on the implementation of the research registry.

2.0 BACKGROUND

2.1 THE AMISH AND MENNONITES

2.1.1 History

The Amish and Mennonites are descendants of 16th century Anabaptists who lived in Europe during a time of Christian church reform.[1–4] Anabaptists were heavily persecuted for their rejection of infant baptism.[1–4] Today, there are three surviving groups: Amish, Mennonite, and Hutterite.

Due to the persecution experienced by the Amish and Mennonites in Europe, many groups fled, accepting an offer of religious freedom from William Penn.[1–4] They settled in what is now known as Pennsylvania. Today, there are Amish and Mennonites living in 23 states and several provinces in Canada. Of these 23 states, Pennsylvania has the second largest populations of Amish and Mennonite individuals.[6] There are an estimated 308,000 Amish and 79,000 Mennonites living in the United States.[6] Today, there are an estimated 59,025 Amish living in Pennsylvania.[7]

The Amish and Mennonites were members of the same practicing faith until the Amish separated from the Mennonites in the 17th century.[2] This separation took place in Switzerland and involved Jacob Amman, a Swiss Anabaptist leader, who encouraged strict faith-based

practices, which included stricter excommunication practices.[2–4] Amman's followers became known as the Amish.[2–4] Despite this separation, these groups still share many of the same beliefs regarding baptism and the bible.[1,2,4]

2.1.2 Culture, Beliefs, Practices

The Amish and Mennonites share a similar history, which includes a way of life rooted in religion.[1] The Amish believe in plain living encompassing simple dress and avoidance of technology and convenience.[1,4] They try to remain separate from the "English" or modern world. The Mennonite also believe in a simple way of life, dressing in a similar fashion to the Amish, however, the Mennonites are not as quick to shy away from technology and modern convenience.[2,4] For example, the Mennonite have been known to drive vehicles and use modern farming equipment. Both the Amish and Mennonite have a strong devotion to community and making decisions based on the community's best interests.

The Amish and Mennonite both speak Pennsylvania Dutch, a German dialect, until they begin school and learn English.[1,2,4] They continue to speak Pennsylvania Dutch among themselves while using English to interact with the world. Children in the Amish community will attend school to grade eight and then they begin full time work, usually on the family homestead.[1,4] There are groups of Mennonites that allow members of the community to attain higher educational advancement.[4]

2.1.3 Healthcare

The Amish value health and taking care of those who have fallen ill.[1] Despite their avoidance of modern technology and their belief that "God created the human body. It should not be tampered with. Medicine may help, but it is God who heals", Amish remain open to receiving modern healthcare.[1] It is rare that an individual will reference the bible to object to medical care.[1]

The Amish do not allow members of their communities to train as physicians because it goes against their beliefs surrounding higher education.[1] For this reason, the Amish must seek medical care from local physicians who are familiar to the community.[1] They will choose healthcare providers based on qualities such as integrity and sympathy; less value is placed on a healthcare provider's training and expertise.[1]

Acceptance of preventative care is variable among families living in the same community.[1] Many Amish families do not want to rely too heavily on "worldly knowledge". An example is vaccination uptake among the Amish. The church does not have set rules regarding vaccinations and other preventative healthcare services.[1] In general, the head of the family makes healthcare decisions, and thus healthcare usage varies among families in the same community.[1]

Despite their willingness to seek modern medical care when needed, this group opposes social security and insurance benefits.[8,9] They are exempt from these government programs based on religious beliefs.[8] Without medical insurance, Amish and Mennonites must pay out of pocket for medical care. The exponential growth of the costs of healthcare in the United States creates a financial burden for many of these families.[8,9] To mitigate these financial challenges, communities will contribute funding for a family's medical bill.[8,9]

Many Amish communities have a means of managing these medical costs referred to as Amish Medical Aid.[8,9] This is a program run by a board of Amish men, consisting of a chairman,

a vice chairman, and four treasurers.[8] Many communities will charge families a fee to be a member of this aid program. A study in Lancaster reported a fee of $125 for a single person and a fee of $250 for a family (children under 18 years old).[8] When an individual receives a major-medical bill (defined as necessary hospital care) they contact an Amish Medical Aid treasurer who will arrange reimbursements with the family or a payment plan with the medical center.[8] Typically, the individual/family is expected to pay 20% of the bill and the Amish Hospital Aid will pay the remaining 80%.[8] If the family is unable to pay the 20%, then they may rely on community donations, called alms.[8] Additionally, many Amish communities have a Disability Relief Aid program, which is organized in a similar manner to the Amish Medical Aid. This fund helps families afford wheelchairs, ramps, and other rehabilitation services.[8]

Other communities rely solely on alms, or donations, to aid families with burdensome medical bills.[8,9] Families are encouraged to donate 10% of their annual income to the church.[8] The church is then able to distribute funding as needed.[8] Both Amish and Mennonite communities have self-sufficiency in their financial healthcare management.

The Amish and Mennonites have also been known to negotiate special price arrangements with hospitals, diagnostic labs, and insurance companies. Typically, families will be given a discounted rate. Additionally, clinics such as the Clinic for Special Children, in Strasburg, PA, raise money the community and through grant funding to provide care to the community.[10]

2.1.4 Genetics

The Amish and Mennonite communities of western Pennsylvania are unique because they are isolated both geographically and socially. These groups originally migrated as a small

group from Europe.[2–4,11] Since this first settlement, there have been additional migration events within North America that have resulted in many distinct communities.[2–4,11] These events lead to genetic founder effects and genetic bottleneck effects.[2] Genetic founder effects are defined as the loss of genetic variation when a new population is established as a small group of people separates from a larger one.[2] Genetic bottleneck effects are defined as the loss of genetic variation when a population size is reduced.[2] The small founding populations result in genetic homogeneity and increased clustering of autosomal recessive mutations in subsequent generations.[2,3] Ultimately these founder and bottleneck effects are exacerbated in the Amish and Mennonite communities by inbreeding and a lack of genetic inflow.[2,3] Additionally, there have been many successive migrations within North America. Specific founder mutations explain the prevalence of different genetic conditions within each community and family group. This means that families and communities will have a clustering of certain genetic conditions, while the prevalence among the Plain people as a whole remains low.[3]

The population's genetic structure, social isolation, inbreeding, large family sizes, virtually null misattributed paternity, and well-maintained genealogic records, make studying genetic disease more straight forward in the Amish and Mennonite communities.[4,11] In 1961, Jackson and Carey were the first to report on a single gene disorder in the Amish.[11] This was a progressive form of muscular dystrophy, called limb-girdle muscular dystrophy. Following this 1961 diagnosis, several cases of phenylketonuria were described.[11] These clinical observations led to genetic studies among the old order Amish in Lancaster, Pennsylvania and Holmes County, Ohio.[11] The genetic studies began in 1962 and were led by Victor McKusick, a geneticist from John Hopkins School of Medicine.[11] McKusick and his colleagues described over thirty Mendelian genetic disorders in the Amish.[3,11] For example, in 1967 McKusick and

colleagues identified Troyer syndrome, an autosomal recessive form of hereditary spastic paraplegias.[12] Researchers surveyed 20 cases with distal muscle wasting beginning in childhood prior to disability. McKusick identified that this was a unique form of spastic paraplegia. An extensive pedigree was taken and suggested an autosomal recessive inheritance pattern based on descent from a common ancestor. In 2002, McKusick and colleagues were able to map Troyer syndrome to chromosome 13q12.3 and identified a frameshift mutation in *SPG20* using DNA sequence analysis that was not available when the syndrome was identified in 1967. [13]

The original genetic studies of the Amish and Mennonite populations traced these conditions through identity by descent, which occurs when the same genes are traced back through common ancestors.[3] Since this research began over half a century ago, technological advancements in genome sequencing have enabled researchers to identify the cause of disease at a molecular level resulting in a new research shift with a focus on treatment of rare recessive conditions.[3] Phenylketonuria is an autosomal recessive condition that is seen in the Amish and Mennonite populations. There are five reported mutations in the Plain Communities.[14] Individuals with Phenylketonuria have accumulation of the amino acid phenylalanine in their bodies, which if untreated will cause intellectual disability.[15] Phenylketonuria is treated by restricting foods with phenylalanine.[15] A drug called Kuvan has the potential to increase phenylalanine tolerance through stimulation of the phenylalanine hydroxylase enzyme, which converts phenylalanine into tyrosine.[15] However, Kuvan is only beneficial for patients who have certain mutations that yield residual enzyme activity; a mutation causing complete loss of protein function, such as a deletion, will not benefit from the drug intervention.[15] This is an example of identifying the cause of disease at the molecular level which can result in targeted treatment of rare diseases.

Despite their way of life and guarded attitude toward modern technology, the Amish and Mennonite communities have continued to participate in clinical research.[3] These communities hope that better knowledge of diseases affecting members of their communities will result in better treatment and reduced suffering. The knowledge gained from studying the Amish and Mennonite populations has improved understanding about genetic diseases that impact these communities.

2.2 CLINIC FOR SPECIAL CHILDREN

The Clinic for Special Children was founded in 1989 by Dr. D. Holmes Morton, and his wife Caroline, in Strasburg, Pennsylvania.[16] Dr. Morton recognized the need for a clinic based on his experiences treating Amish children with glutaric acidemia type-1 and maple syrup urine disease while in training at the Children's Hospital in Philadelphia.[16] The clinic was founded with the aim of providing local and affordable services to the Amish and Mennonite families living in eastern Pennsylvania.[16] Since its beginnings, the clinic has expanded to integrate both a biochemical and molecular genetic testing laboratories which have provided extensive research opportunities.[16] The clinic is an example of positive healthcare outcomes stemming from early disease detection, community awareness, and affordable care.[10] For example, prior to the Clinic for Special Children, infants with maple syrup urine disease (MSUD) and glutaric acidemia, type 1 would present for care at hospitals after there was neurologic damage or they were critically ill.[10] "Childhood morality from maple syrup urine disease was 39%, and 94% of Amish children with glutaric acidemia, type 1 were fully disabled by metabolic strokes before age 2".[10] Prior to the Clinic for Special Children, care was inconsistent, parent education was poor and a great

amount of money was spent on medical emergencies.[10] The Clinic for Special Children provided a local source of healthcare with physicians who were familiar with rare metabolic conditions. Those affected received care before medical emergencies reducing hospitalization costs for families. [10]

Additionally, the clinic has demonstrated the utility of genomic research generating positive healthcare outcomes. Research initiatives through the Clinic for Special Children have resulted in the identification and treatment of several complex genetic diseases.[10] Since the clinic has a molecular genetics laboratory, they have identified select genetic mutations found in Amish and Mennonite communities.[16] Their website has a list of Amish and Mennonite mutations that their laboratory is able to identify.[16] This has allowed for targeting screening for conditions such as tyrosinemia type 3, congenital nephrotic syndrome, and phenylketonuria.[16] This clinic model incorporates both primary care and a research center, providing an innovative example of translational medicine in practice.[10]

The clinic began treating patients with glutaric academia, type 1 and maple syrup urine disease, which affect 1 in 400 Amish and Mennonites.[10] Staff developed specialized protocols and testing to decrease hospitalizations and their associated costs.[10] Since the clinic began, services have expanded to meet wider community needs.[10] The clinic has demonstrated success with increasing diagnostic efficiency and reducing lab costs by incorporating molecular technologies in the primary care setting. In 2010, the clinics 1.5 million dollar budget saved 20-25 million dollars in community medical costs.[10] The clinic provides a successful example of the benefits of investing resources in primary care and molecular technology to reduce hospitalization costs.[10]

Figure 1. Clinic for Special Children in Strasburg, PA.

2.3 CLINIC FOR THE PLAIN COMMUNITIES

Figure 2. Logo for the Clinic for the Plain Communities through Children's Hospital of Pittsburgh of UPMC.

A collaborative effort of the Center for Rare Disease Therapy and the Division of Medical Genetics at Children's Hospital of Pittsburgh of UPMC, the Clinic for the Plain Communities was developed in 2015 to provide a monthly satellite specialty clinic to Amish and Mennonites living in western Pennsylvania and eastern Ohio.[6] The clinic offers services from Medical Geneticists, Genetic Counselors, and Pediatric Neurologists to both pediatric and adult patients.[6] The clinic has the capacity to see 8-10 patients a month. Bringing services closer to these communities will mitigate the financial burden traveling would otherwise impose on families. Amish, and some Mennonites, do not drive vehicles for religious reasons and therefore must hire drivers.[1] Families we have worked with report a cost of one dollar per mile traveled. Although the Clinic for the Plain Communities is not a primary medical home, the goal remains to improve and build relationships with the Amish and Mennonite communities of western Pennsylvania. The clinic has the potential to improve access, community awareness, and research in western Pennsylvania.[6] Additionally, the Clinic for the Plain Communities aims to build collaborative efforts with other clinics serving these vulnerable and underserved populations.

2.4 CONSORTIUM OF CLINICS

Since the Clinic for Special Children in Strasburg, PA opened its doors to the Plain Communities, other clinics have been established: The New Leaf Clinic in Ohio, The Community Health Clinic in Indiana, DDC Clinic Center for Special Needs Children in Ohio, Central Pennsylvania Clinic – A Medical Home for Special Children and Adults in Bellville Pennsylvania, and LaFarge Clinic in Wisconsin.[17–21]

These clinics were created to improve access to care, decrease medical cost burdens, educate communities, and increase knowledge of genetic disorders affecting the Plain Communities. In 2013, a Translational Medicine in Plain Populations Conference brought many of these clinics together, along with clinicians and researchers from other universities and medical centers.[22] The conference has become an annual event that focuses on clinical care and genetic research in the Plain Communities.[22] This conference resulted in collaborative relationships among these clinics, which eventually resulted in the formation of a consortium of clinics, which currently includes 7 clinics. This consortium is new and still developing a blanket missions and goals statement.

The summer 2016 conference provided clinics, physicians and researchers the opportunity to learn current research practices for diagnosis and treatment of genetic diseases in the Plain communities.[22] Additionally, the conference provided a platform for a discussion on resources for genome/exome projects and barriers that hinder medical care in these communities.[22] It is expected that collaborative efforts will continue as this consortium of clinics and researchers continues to grow and define its future goals for Plain Community medical care. One such effort is the development of a program of research and therapeutic development for GM3-synthase deficiency, a rare autosomal recessive disorder characterized by abnormal brain development and seizures.[23] Collaborative studies are also underway to delineate the natural history of the Amish variant of propionic academia, which is also a rare autosomal recessive disorder characterized by cardiomyopathy and seizures in the infantile period.[24]

2.5 VULNERABLE POPULATIONS RESEARCH CONSIDERATIONS

Today, a researcher must submit a proposal to an Institutional Review Board (IRB) following many guidelines for research practice if patients will be approached to participate in the research. The IRB is much like a "gatekeeper" ensuring that vulnerable populations, such as the Amish and Mennonite, are not taken advantage of in the conduct of research.[25] A vulnerable population can be defined as "those who are not only particularly sensitive to risk factors but also possess multiple cumulative risk factors. They are more likely than others to develop health problems as a result of exposure to risk or have worse outcomes from these health problems than the rest of the population".[26]

The need to protect vulnerable populations stems from a negative history where these populations were either harmed, manipulated, or coerced by researchers.[27] To protect human research subjects from harm, standard practices and research guidelines were developed as outlined in the Belmont Report, which was published by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1979.[27] There are three key elements of this report: 1) Respect for persons, 2) Beneficence, and 3) Justice. Respect for persons refers to the protection of a person's autonomy and information collected during research.[27] Beneficence highlights the need to maximize benefits and minimize harm, promoting welfare of participants.[27] Justice describes the need for study recruitment and study benefits to be equally attainable by all participants.[27] These core principles are important for all human subject research.

Wilson and Neville describe a framework for vulnerable population research.[28] The framework consists of the 4 Ps: Partnership, Participation, Power, and Protection. Partnership involves building relationships with the population or community of interest.[28] This relationship

needs to be built on respect and trust.[28] Participation requires the continued involvement of those research participants in the research process and design.[28] Additionally, this can include involving key members and stakeholders for advice and guidance in the planning process[28]. Power relates to self-reflection on the part of the researcher.[28] It is important for researchers to reflect on their own beliefs, values, and practices that may impact their research with any given community.[28] Lastly, protection means avoiding exploitation. This is achieved when one keeps the needs of the community in mind, respects and incorporates the community's traditions and respects the knowledge that the community can bring to the study.[28]

The aim of vulnerable population research should always be to benefit the community of interest and improve the inequalities in health burdens, experiences, and outcomes.[25] Continually incorporating a vulnerable population's values, expertise, and needs into the research design will create a culturally safe place for research.[25]

2.6 RESEARCH INITIATIVES AT THE CHILDREN'S HOSPITAL OF PITTSBURGH OF UPMC

In addition to building relationships with the Amish and Mennonite families of western Pennsylvania through the Clinic for the Plain Communities, Children's Hospital of Pittsburgh of UPMC is engaged in several research initiatives.

The Medical Genetics and Neurology clinical and research teams at Children's Hospital of Pittsburgh of UPMC identified four different Amish families with mitochondrial respiratory chain disorders which were never reported before in the Amish population.[29] Two of these families had mutations in mitochondrial encoded genes and the other two had mutations in

nuclear encoded genes.[29] Further studies on extended family members of the Amish index patient from Northwestern Pennsylvania diagnosed with MELAS syndrome (Mitochondrial Encephalopathy, Lactic Acidosis, Stroke-like Episodes), due to a mitochondrial DNA (mtDNA) mutation (m 3243AA>G), were performed and 13 additional family members tested positive for the same mutation.[29] Additionally, the team assessed the effectiveness of a community educational intervention.[29] These patients represented the first report of mitochondrial respiratory chain deficiency in the Old Order Amish or any of the Plain People.[29] It is also the first study to show that maternally inherited mitochondrial disease may be under-recognized in the Amish community and other Plain communities and that educational interventions are well received and effective tools.[29]

Most recently, the Medical Genetics Research team at Children's Hospital of Pittsburgh of UPMC has developed a study for Whole Exome/Genome research in the Plain Communities. The study aims to identify genetic disorders in patients who have symptoms suggestive of a hereditary disorder but for which the etiology has not been defined.[30] Identifying disease etiology, through Next Generation Sequencing (NGS) technology, will aid in appropriate decision-making regarding management and therapies.[30] Additionally, the study aims to assess the presence of disease alleles in these communities as compared to disease alleles in other Amish communities, some of which may be new.[30] Detecting the presence of known or novel disease alleles will provide information on disease risks among each distinct community in western Pennsylvania.[30] Lastly, the exome studies will be used to track population variations as communities have moved throughout the eastern and upper mid-western United States.

The long-term goals of these research initiatives at Children's Hospital of Pittsburgh of UPMC are to increase accessibility to genetic health information, by lowering costs and

increasing efficiency of testing, and it will help researchers better understand genetic disease risks in these communities. Future research aims to strengthen relationships with the Amish and Mennonite and continue to expand medical care for patients with rare genetic disorders in these communities.

2.7 COMMUNITY BASED RESEARCH REGISTRIES

Use of research registries to accumulate information about specific disease has been increasing in the last few years, however, researchers have long-described the value of using community based research registries for collecting health information and for improving access to health research.[31,32] For example, some researchers suggest community-based research registries could provide "epidemiologic utilization, prevention, and outcomes data that would help to improve quality of life and clinical outcomes for patients". [31,33]

Janosky et al, report on the implementation of The Center for Primary Care Community Based Research designed for the purpose of community based retrospective research.[31,33] Participant recruitment was conducted in Pittsburgh through The Center for Primary Care Community-Based Research at the University of Pittsburgh. Potential participants were approached at five medical centers for underserved communities and at community venues, such as health fairs, churches, and festivals. Participants were asked to fill out a questionnaire providing researchers with self-reported medical history, family history and medication information. Results show a difference in rates of various conditions, such as high blood pressure, in participants recruited through medical centers versus community venues, suggesting a need for multi-modal recruitment methods. Collection of comprehensive medical data may

have been impacted by use of self-reporting in this study. Avoiding this approach is important if the purpose of the registry is to recruit participants to future research studies. Accurate medical information is needed to insuring appropriate individuals are being ascertained for future research studies.

Bishop et al, developed a community research registry for recruiting underserved minorities for health research.[32] Potential participants were recruited to the research registry through community health fairs and were asked to fill out a survey. Limited information was published on their registry recruitment approach, whether registry data was self-reported, and limitations of the registry development. The aim of the study was to assess the recruitment of registry participants for future research studies. Five studies contacted 2,301 participants from the registry who were appropriate for the given study. Of those contacted, 1,130 were reached and 51.9% were scheduled to participate in one of the five studies. Of those 51.9%, 60.8% completed a study appointment. These data show that a community research registry can lead to participation in health research and has the potential to create equal opportunities for races currently underrepresented in the study population.

The research presented above on community based research registries support the development of an Amish and Mennonite Research Registry as a means for increasing opportunities for health research in these communities, and may lead to improved understanding of health concerns specific to a community. Bishop et al, demonstrated a community research registry can lead to participation in future research studies in underrepresented populations.

Currently there is limited information on community research registry recruitment design for vulnerable populations. Developing an Amish and Mennonite research registry will provide a culturally appropriate model for recruiting vulnerable and underserved populations for research.

The registry will provide future research opportunities for this underrepresented population in western Pennsylvania.

3.0 MANUSCRIPT

3.1 ABSTRACT

Keywords: Amish, Mennonite, Plain Communities, Research Registry, Genetics

The Amish and Mennonites of western Pennsylvania are genetically isolated religious communities that are disproportionally burdened by genetic disease due to founder and bottleneck effects from their European migration in the 17th century. Research studies to better understand the types of conditions in the communities, the natural history of these conditions, as well as health care needs of these communities, will allow for more targeted delivery of appropriate healthcare interventions. However, barriers exist for identifying and ascertaining appropriate members of the Plain Community for research studies. The Plain Community is considered a vulnerable population because of their unique cultural identity, geographical isolation and limited utilization of healthcare. Vulnerable groups are often difficult to reach, however, there has been support for community based research registries as a way to address disparities for access to and participation in research. An Amish and Mennonite Research Registry was developed in western Pennsylvania to diminish these barriers and provide a platform for contacting willing members of the Plain Community for participation in future research projects that may positively impact future medical care, as well as the general care in their communities. Improving working relationships among Amish, Mennonites, and researchers

has public health significance because it could improve health care delivery to the Plain Communities in western Pennsylvania. We developed a culturally appropriate approach for recruiting and consenting members of this vulnerable population. This paper reports on the development and implementation process of the research registry and its public health importance.

3.2 INTRODUCTION

The Amish and Mennonite communities of western Pennsylvania are unique because they are isolated both geographically and socially. These groups are descendants of the 16th century Anabaptists living in Europe during a time of Christian church reform.[1–4] Due to the persecution that the Amish and Mennonites faced in Europe, many groups fled, accepting an offer of religious freedom from William Penn, settling in what is now known as Pennsylvania.[1–4] Today, there are Amish and Mennonites living in 23 states and several provinces in Canada.[6,34] Of these 23 states, Pennsylvania has the second largest populations of Amish and Mennonite individuals.[6,34]

These migration events lead to genetic founder effects, genetic bottleneck effects, and virtually zero genetic inflow, due to cultural preferences to marry within the community.[1–4,11] The result has been an increased burden of specific genetic disorders[3]. Specific founder genes explain the prevalence of different genetic conditions within each community and family group[3]. This means that families and communities will have a clustering of certain genetic conditions, while the prevalence among the Plain People as a whole remains low.[3] Understanding the

specific needs of each family and community group is important to enable delivery of comprehensive and specialized care.

The Amish value health and taking care of those who have fallen ill. [1] Despite their avoidance of modern technology, Amish and Mennonites remain open to receiving modern healthcare. Although these communities are willing to seek medical care when needed, they oppose social security and insurance benefits. [8,9] Without medical insurance, Amish and Mennonites must pay out of pocket for medical care. The exponential growth of the costs of healthcare in the United States creates a financial burden for many of these families.[8,9] To mitigate these financial challenges, communities will contribute funding for a family's medical bills. Many Amish communities manage medical costs through Amish Medical Aid.[8,9] This is a community program requiring members to pay a fee and when an individual receives a major hospital bill (defined as necessary hospital care) they contact an Amish Hospital Aid treasurer who will arrange reimbursements with the family or a payment plan with the medical center.[8,9] Many also rely on community donations called Alms.[8,9]

Due to the geographical isolation, the burden of specific complex diseases, and the lack of medical insurance in the Plain Communities, clinics were developed to serve this vulnerable population. The Clinic for Special Children in Strasburg, PA was the first clinic to open its doors to Amish and Mennonite families. Since this time, other clinics have been established to improve access to care, decrease medical cost burdens, educate communities, and increase knowledge about genetic disorders affecting the Plain Communities. These clinics have joined a consortium, along with interested research institutions, to build collaborative efforts for improving care in these communities.

Research studies to better understand the types of conditions in the communities and the natural history of those conditions, as well as needs assessments within these communities, will allow for more targeted delivery of appropriate healthcare[3]. Currently this need is being addressed in eastern Pennsylvania by the Clinic for Special Children in Strasburg.[3,9,10] This organization has provided primary care medicine, and conducted research to improve access and quality of care for these Plain Communities.[3,9,10] There is a need for a similar understanding and relationship with the Plain Communities of western Pennsylvania.

Currently a barrier exists for identifying and ascertaining appropriate individuals within the Plain Community in western Pennsylvania for new research studies. This is largely due to their social and geographical isolation related to religious and cultural practices.[1] Improving research and understanding of Plain Communities has the potential to improve early diagnosis, interventions, and clinical outcomes.[3,9,10] Creating an ongoing registry will break down these barriers and provide a platform for contacting willing members of the Plain Community for participation in future research projects that may positively impact their medical care, as well as the general care in their communities. Bishop et al, developed a community based research registry for recruiting underserved minorities for health research.[32] Potential participants were recruited through community health fairs and were asked to fill out a survey. Researchers assessed the recruitment of registry participants to future research studies. Results show that a community research registry can lead to participation in health research and has the potential to create equal opportunities for populations currently underserved.

The aims of the registry development were to devise a culturally appropriate method for contacting and consenting willing members of the Plain Community. Additionally, researchers aimed to construct a detailed extended family pedigree for each consented participant and to

collect a detailed medical history. The final aim was to create a platform for identifying and contacting appropriate members of the Plain Community for participation in future.

3.3 REGISTRY AND CONSENT DEVELOPMENT

3.3.1 Ethical Considerations

The Institutional Review Board of the University of Pittsburgh approved this study (PRO16030311-Appenix A). Informed consent was obtained from all participants.

3.3.2 Inclusion Criteria

All available Amish and Mennonite men and woman were invited to participated in the Research Registry and to consider enrolling their children, as well. Recruitment was broad because of the potential to enroll in a variety of future studies, including population variant studies, undiagnosed disease studies and community needs assessments. We recruited subjects who were unable to provide direct consent through proxy consent because there is limited risk and there is potential for recruitment to a future research study that may positively impact their medical management. Children under the age of 18 required a parent or legal guardian who spoke English to act as an interpreter for assent and to formally consent to registry participation.

3.3.3 Exclusion Criteria

We did not have the resources to offer interpreters who spoke Pennsylvania Dutch, thus we excluded all those 18 years and older who did not speak English. It is understood that Amish and Mennonite children do not learn English until they start school.

3.3.4 Timeline

The research team spent roughly two months developing the recruitment strategy, connecting with the Mercy County Health Department, obtaining support from Dr. Holmes Morton, who has extensive experience with this population, designing the registry brochure, and writing the IRB protocol. The IRB protocol was reviewed by the full review board because of the unique vulnerability of the Amish and Mennonite communities. During the IRB review period, PhenoTips software was downloaded behind the institutional firewall.[35] The team began consenting patients immediately upon IRB approval. Over the course of 7 months we have consented five participants to the registry and have had four individuals decline participation.

3.3.5 Avenues for Participation Recruitment

Recruitment focused on avenues that are part of the Amish and Mennonite communities, such as existing healthcare programs and public health programs. Dr. D. Holmes Morton provided a letter of support for our recruitment design based on his experiences with recruitment in the Plain Communities in Eastern Pennsylvania (Appendix C). Participants were identified

and recruited through three main avenues: inpatient consultations, family and friend referrals, and scheduled community educational events.

Inpatients were identified through the in house MEDIPAC system. This system has a religious preference filter, which allows for easy identification of the majority of Amish and Mennonite in-house patients. Individuals were ascertained through Children's Hospital of Pittsburgh of UPMC; however, IRB approval was obtained also for Magee Woman's Hospital of UPMC, UPMC Presbyterian, UPMC Shadyside, and UPMC Horizon. The patients' attending physician was contacted to assess feasibility and acceptability of approaching their patient about the Research Registry. For cases where an inpatient had a genetics consultation, the genetics consultant asked the family if they would be interested in learning more about a Research Registry. If the potential participant expressed interest, then a referral was made to the research team.

All individuals approached by the research team were provided with a culturally appropriate, plain language brochure regarding the registry (See Appendix D). The consent form was reviewed in detail and patients had opportunity to ask questions. Individuals who signed a consent form to participate in the Research Registry were asked to inform other family and community members who were not seen at the time of consent about the registry. Our contact information was provided, as well as extra registry brochures. When family or community members contacted the research team, we discussed the Research Registry with these individuals.

The Mercer County Public Health Department works closely with the Amish and Mennonite communities. The health department regularly hosts educational and health outreach events for these communities. Our research team has developed a relationship with the Mercer

County Health Department, and with their permission and cooperation, the research team was present at an Amish Safety Day event where we provided information on the Clinic for Plain Communities and Children's Hospital of Pittsburgh of UPMC and will be present at planned future events when Amish and Mennonite individuals will be in attendance. The IRB protocol was not yet approved at the time of the 2016 Safety Day so we could not promote the research registry. In future, brochures and information on the Research Registry will be provided. Community members are encouraged to contact the research team in future if they are interested and have an opportunity to consent on site if interested.

Figure 3. Staff and researchers attending Amish Safety Day in Mercy County, PA[6].

3.3.6 Brochure Development

The Research Registry brochure was designed to provide participants with information on what it means to be a part of a Research Registry. It was also designed as a resource to pass along to spouses, family, and community members. The brochure included topics such as

benefits for joining, what is required, who can participate, privacy, cost, compensation, and how to withdraw. The aim when designing the brochure was to keep sentence structure simple and the literacy level at the eighth-grade. The literacy level was evaluated using the Coleman-Liau online readability formula. The Research Registry brochure was limited to two pages of the most important information from the consent form, with the intent to make the brochure appear manageable to read. The design of the Research Registry brochure was uncluttered, incorporated white spaces, and an obvious path for the reader to follow, helping with ease of reading. Headings were used to emphasize important topics. We also made sure the Research Registry brochure content was culturally appropriate. Images of humans were avoided because many Amish and Mennonite avoid personal photographs.[1] Farming and simple country scenes are familiar to the Plain Communities; therefore, a single image of a farm and flowers was chosen for the front cover. The Amish and Mennonites are family and community oriented; therefore, family and community members were referenced in the brochure. A simple, culturally appropriate color scheme was also chosen[1]. The full brochure can be found in Appendix D.

3.3.7 Informed Consent

Potential participants were educated about the intent of the registry and written informed consent was obtained to allow for collection and storage of information in the registry for an indefinite period of time. Participants were informed about what it means to be a part of the registry and the potential for contact and recruitment to future research studies.

Individuals 18 years and older provided consent for themselves (Appendix B1.1). Individuals younger than 18 years, required consent from a parent/guardian. The child consent form (Appendix B1.2) had an assent section for participants 14-17 years of age. In these

communities, children less than 12 years of age do not speak fluent English and children are integrated into fuller participation in community activity at an older age.[1] Prior to the chosen age of assent, children do not typically participate in decision making and therefore asking them to decide whether to join the Research Registry would be beyond what they are expected to do at that age.[1] At age 18, participants must re-consent as an adult to remain in the registry.

Individuals who have limited ability to provide informed consent due to intellectual disability can have their parent sign on their behalf. Based on Pennsylvania law, no other guardian is allowed to consent for the disabled individual unless they have been legally authorized to consent for research studies for the individual with a disability. The Principle Investigator or Co-Investigators determine if the subject has the capacity to provide assent to participate in the study.

In these communities, there is a strong value placed on participation in activities for the common good of the community.[1,36] To minimize the risk that an individual would feel obligated to participate in the registry based on potential for common good, consent is obtained in a private setting. Individuals are also informed that their participation and/or their child's participation is voluntary and that choosing not to participate does not impact their medical care or their relationship with any UPMC facility provider.

An Excel spreadsheet was used to track the number of times a potential participant was approached regarding the registry. The document also tracked the date of consent, assent, and re-consent. This Excel spreadsheet is housed on a secure server behind the institutions firewall and access is limited to research team members.

3.3.8 Data Collection

3.3.8.1 PhenoTips Database

PhenoTips was used by the research team to house participant information. It is an open source, searchable software program designed to provide a platform for compiling and analyzing phenotypic information of patients with genetic disorders.[35] It was developed by Marta Girdea, PhD, and colleagues at of the University of Toronto and the Hospital for Sick Children in Toronto.[35] It provides physicians and researchers an easy to use, searchable program with standardized phenotypic vocabulary and a platform to store most other types of patient data (pedigrees, laboratory values, etc.) in a standard format.[35]

The database contains multiple sections that allow a researcher to select from standard menus, record notes, and upload files.[35] The database was designed to support the needs of both clinical geneticists and researchers, thus some of the standard fields and sections may be more suited to a clinical setting versus a research setting.[35] The research team has flexibility to use all sections because of the broad patient data being collected. Data collection is broad as to not limit information that may be important for inclusion into future research studies. The following sections are included in the database[35]:

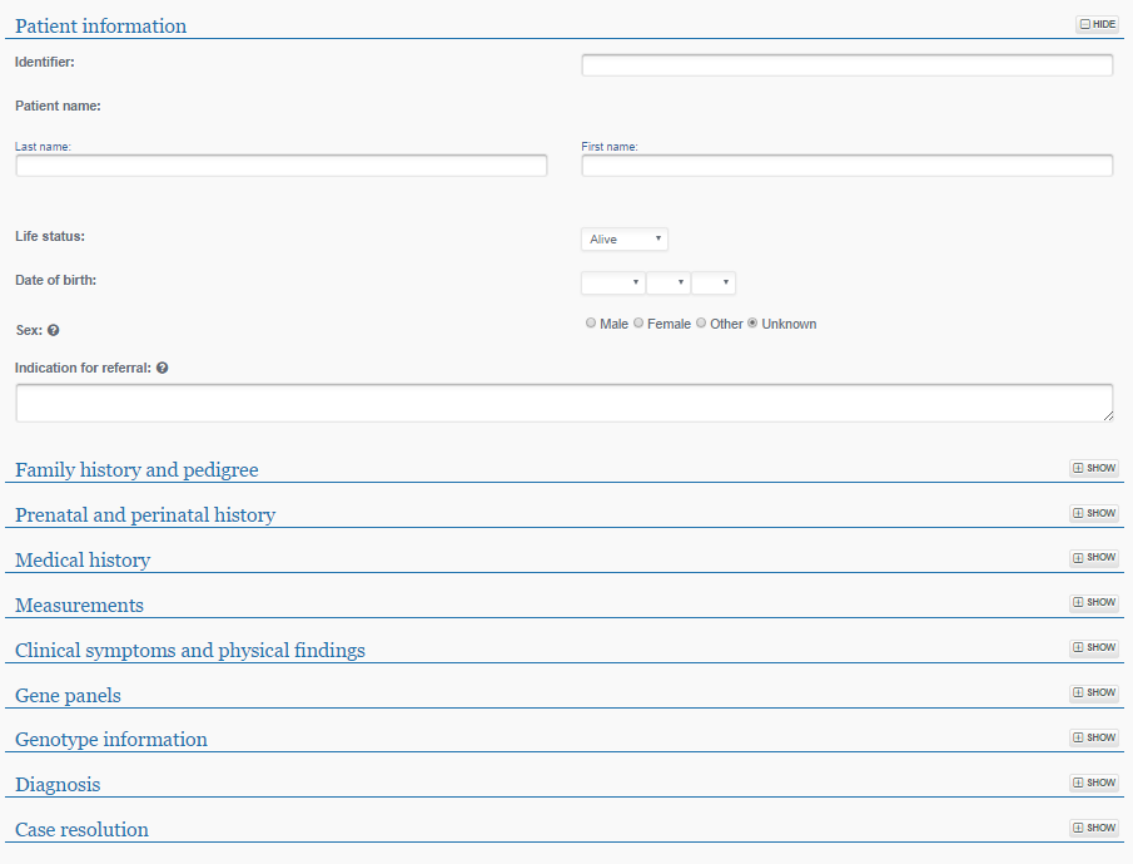

Figure 4. PhenoTips main patient profile categories.[35]

a) *Patient demographic information*: patient age, date of birth, gender, research identifier.

b) *Family History and pedigree*: a pedigree (uploaded or constructed using the database draw function), maternal and paternal ethnicity, consanguinity, inheritance patterns, list of known disorders and phenotypes in the family.

c) *Prenatal and perinatal history*: gestational at delivery, assisted reproduction details, APGAR scores, pregnancy history, prenatal development, delivery, neonatal growth parameters.

d) *Medical history*: development, allergies, ages of onset, medications, previous medical records (can be uploaded).

e) *Measurements*: standard height, weight, and head circumference, as well as more detailed measurements such as ear length. Multiple entries can be mapped over time.

f) *Clinical symptoms and physical findings*: ability to select standardized phenotypes. Fields are organized into major body systems; growth parameters, craniofacial, eye defects, cutaneous, cardiovascular, respiratory, musculoskeletal, gastrointestinal, genitourinary, behavior and cognition, neurology.

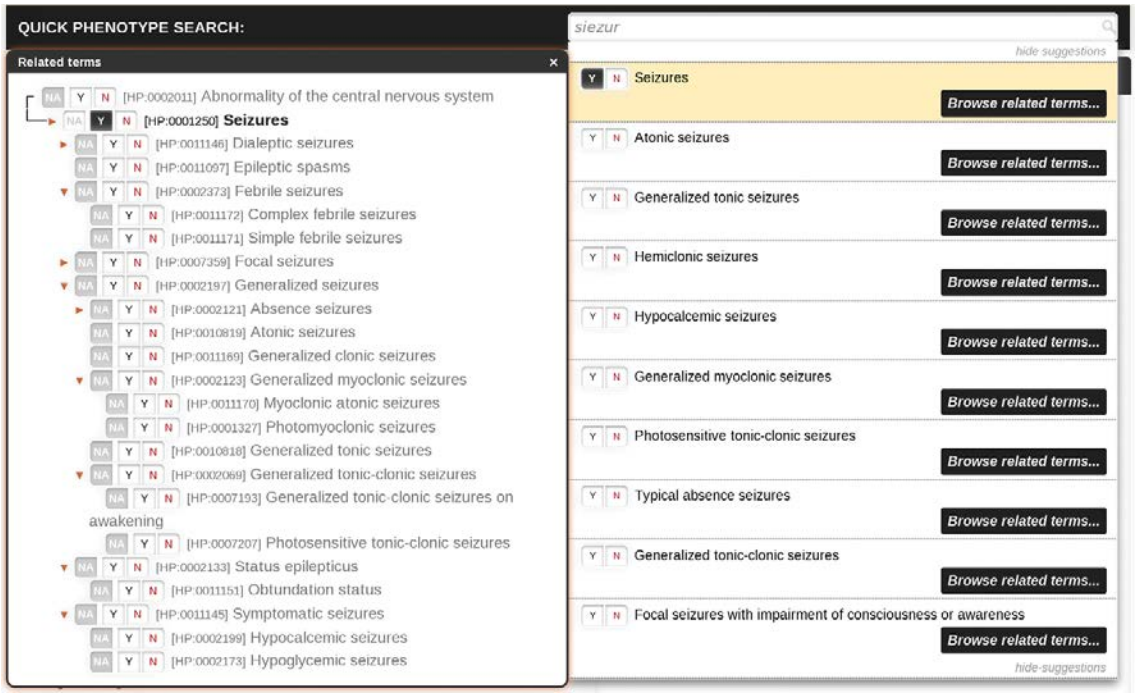

Figure 5. Example of the detailed clinical symptoms fields.[35]

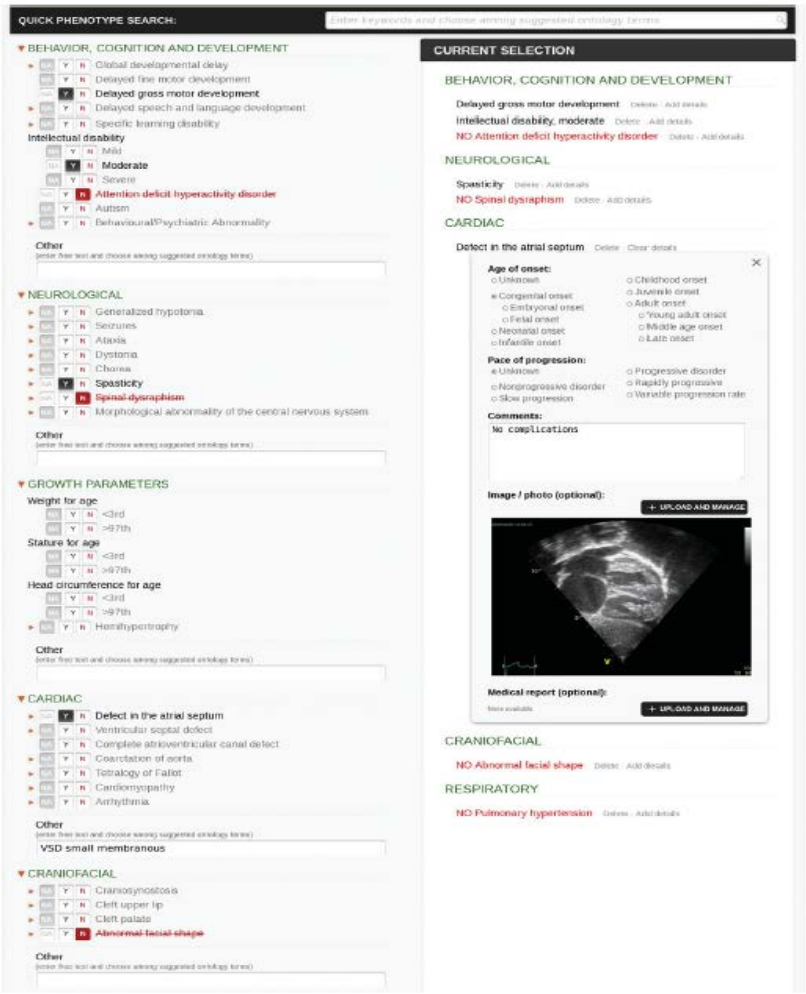

Figure 6. Example of several of the clinical phenotype fields.[35]

g) *Gene panels*: suggested list of genes extracted from the phenotypic descriptions provided

h) *Genotype information*: Genes tested and their results, including detailed descriptions of test (i.e. sequencing, del/dup) and variants discovered.

i) *Diagnosis:* results from automated OMIM searches that match phenotypic descriptions provided.

PhenoTips software was downloaded on an independent server, behind the institutional firewall. Access to the software was granted to select research computers within the Division of Medical Genetics, Children's Hospital of Pittsburgh of UPMC. The software is fully HIPAA compliant and designed to support data privacy. Only individuals granted access to the registry have access to the information.

The design of the database facilitates research and registry development because it supports different user roles and different levels of access. There is "viewer" access which allows an individual to browse data but not modify it. This viewer mode would be appropriate when adding IRB-approved collaborators who wish to contact registry members about their study. There is "contributor" access which enables an individual to modify and contribute their own patient/participant profiles. The "data administrator" access allows an individual full access with the ability to modify and remove data. Lastly, the "server administrator" access allows an individual the same permissions as the "data administrator" however an individual can also grant access to new research members. Individuals accessing the database would be IRB-approved.

The database supports a research registry because it provides easy-to-use filters for sorting through the large volume of participants and identifying individuals who would be appropriate for a future research project. These filters include: authors, owner, creation date, last modification date, date of birth of patient, disorder, phenotypic feature, and gene.

The use of other databases was discussed; however, other databases would have been limiting with regards to the range of data that could be entered, and in some cases, requires defining fields before the breadth of phenotypic information is known. PhenoTips allows for a broad range of data to be entered which is important for the aim of this research registry. Recruitment is broad based because of the potential for participation in a variety of research

studies such as population variant studies, undiagnosed disease studies, and community needs assessments.

The ability to upload or construct a pedigree directly in the database was important to the research team because we wanted participant information all in one place. PhenoTips was the only software program that encompassed these needs. The software was also a free download, which was an added bonus on a limited research budget.

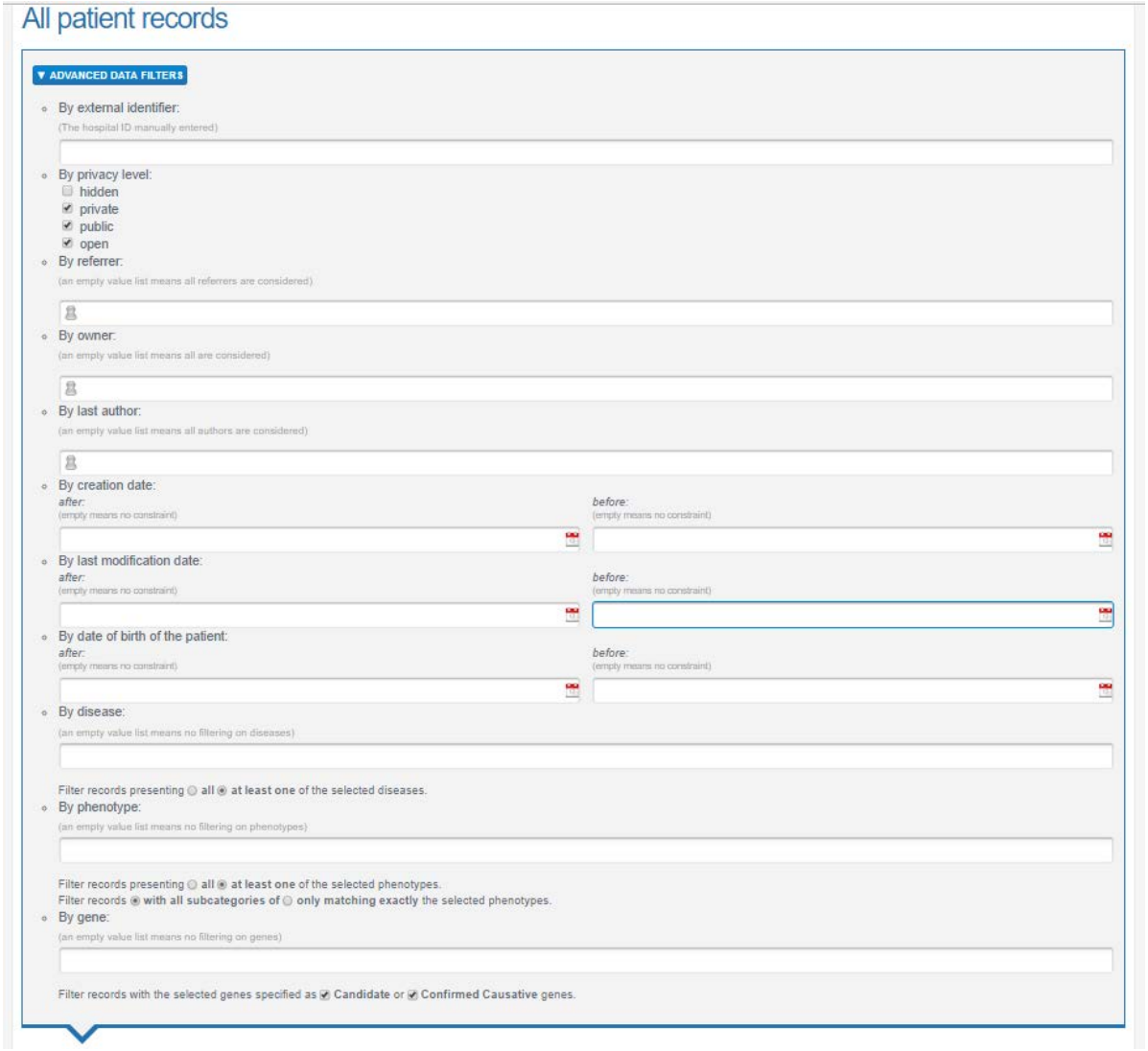

Figure 7. Filters for sorting through registry participants.[35]

3.3.8.2 Pedigree Construction

One-on-one interviews were conducted by primary investigators or co-investigators in a clinical setting following the signing of the consent form by the registrant. The aim was to collect detailed family and reported medical histories. Participants answered questions about themselves and third party first, second, third and sometimes more distant degree relatives. Information learned about participants' relatives was not confirmed by the participant or by medical records. A three to four generation pedigree was constructed on a paper intake sheet. The pedigree was later entered in the Phenotips database, which has a field in each participant profile for pedigree construction.

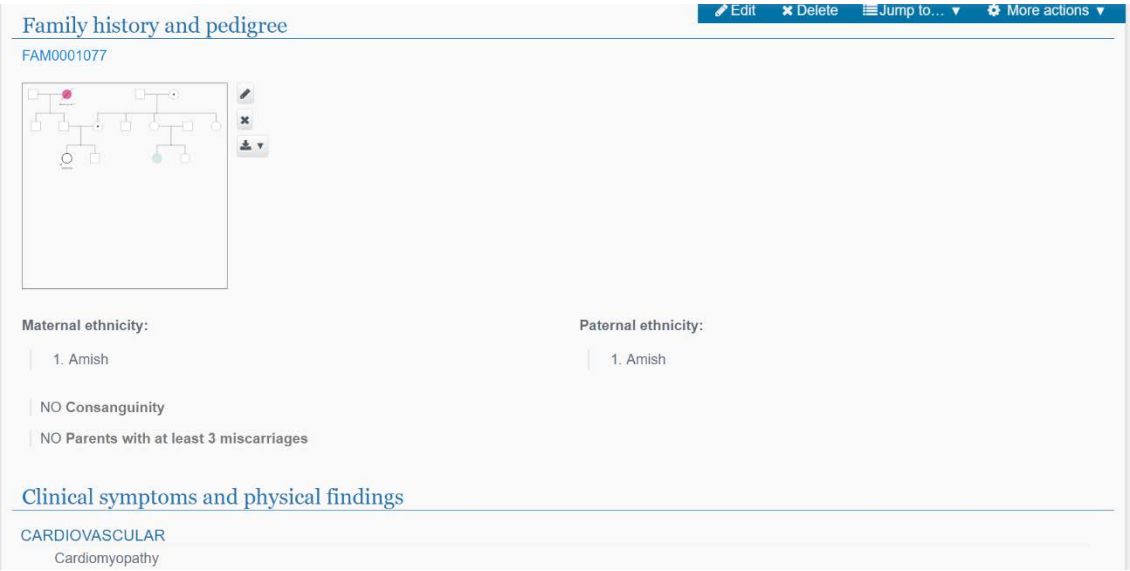

Figure 8. Family history and pedigree field of the patient profile[35].

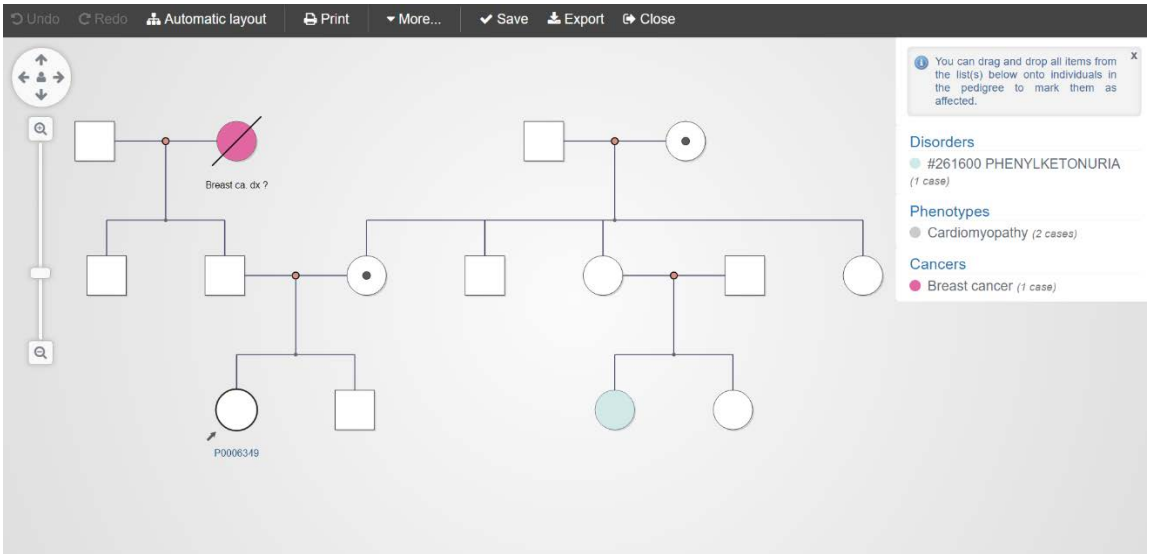

Figure 9. Example of a pedigree drawn in PhenoTips with a legend for family disorders, phenotypes, and cancers[35].

For each family member identified we asked for their first name and maiden names. We also asked about the following list of findings for each individual:

a) Major health concerns; if so, age of diagnosis/onset of symptoms and management

b) Learning difficulties or needing extra help in school

c) Reached milestones at the expected times

d) Birth defect (such as congenital heart defects, extra fingers or toes, neural tube defects)

e) Requiring a special diet at birth because of a metabolic condition

f) Still births or infant deaths

g) Pregnancy losses

h) Cancer diagnosis; if so, type, age, treatment

i) Genetic testing or genetic diagnoses

j) Consanguinity

3.3.8.3 Medical History Collection

After one-on-one interviews, the participant's medical history was confirmed through review of medical records. Medical records were reviewed through the institution's electronic medical record system or through released medical records from an outside institution. The participants UPMC medical records from all facilities were collected. These medical records included clinical notes, inpatient notes, scanned outpatient results, laboratory results, pathology results, diagnostic study results, and imaging results. The information obtained from medical records were recorded in the PhenoTips database.

3.4 DISCUSSION

3.4.1 Creating a Culturally Safe Space

Creating a culturally appropriate approach for recruiting and consenting this vulnerable population was a priority. Researchers educated ourselves on the history, culture, and medical views of the Amish and Mennonite communities. Researchers recognized that creating a culturally safe space was important for dialogue between participants and researchers.[27,28] From this approach, researchers learned of their views, perspectives, and hesitations regarding research registry participation. Consciousness of important cultural differences is reflected in their recruitment approach and our research registry material design.

The Plain Communities value familiarity and long standing relationships when it comes to medical care and education.[1] For this reason, researchers chose to collaborate with the Mercer County Health Department, a known and trusted forum for education and medical outreach for

the Plain Communities. Additionally, support from Dr. Holmes Morton, the founder of the Clinic for Special Children. Dr. Morton is well known and respected within the Amish and Mennonite communities. During interactions with families, to create connections, potential participants were asked if they were familiar with the work being done in eastern Pennsylvania by Dr. Morton. All of those approached were familiar with his work and knew a family or community member who had received care at the Clinic for Special Children. The ability to mention Dr. Morton's support for this work, and his collaboration with other ongoing Plain Community studies at Children's Hospital of Pittsburgh of UPMC, allowed building of the initial trust needed to further discuss our Research Registry.

Literacy level and English as a second language were important considerations when developing written registry materials. Amish and Mennonites speak Pennsylvania Dutch in their community and do not learn English until they begin school.[1,4] Furthermore, Amish community members do not attend school after the eighth grade.[1,4] Writing a consent form at the eighth-grade reading level, which was inclusive of all the Institutional Review Boards requirements was difficult, and it was only possible to achieve a literacy level at the tenth-grade. However, the brochure was designed to be an even easier read and an additional resource informing participants on what it means to be a part of a Research Registry. A grade seven reading level was achieved for the brochure. Further, step-by-step review of the consent form with plain language explanations was provided to those approached, if needed.

During interactions with potential participants, researchers remained conscious of language used and the examples provided. For example, Amish and Mennonite communities keep a directory of families.[1] These community directories are used to keep track of and contact

families or members of a given community.[1] Comparison of their directories to the research registry were provided, both are a way to identify and contact members of the community.

3.4.2 Willingness to Participate

The Amish value health and taking care of those who have fallen ill[1]. Despite their preference to avoid modern technology, if possible, and their belief that "God created the human body. It should not be tampered with. Medicine may help, but it is God who heals", Amish remain open to receiving modern healthcare.[1,3] It is rare that an individual will reference the bible to object to medical care[1]. These values were evident when speaking with potential participants. Many of those approached were open to the idea of participating in research. These families were quite familiar with the modern healthcare system and understood, first hand, the benefits from care for complex health conditions their families had received. Additionally, many of the potential participants had participated in various previous research studies. It was encouraging to witness their continued interest in medical research. This was not their first experience outside the community. Future interactions with other community members may be different because many members of the Plain Community have remained isolated from modern healthcare and therefore researchers may encounter individuals in this population to whom the idea of research and healthcare technologies may be a foreign concept. The Amish and Mennonite populations of western Pennsylvania are underserved and less connected to modern medicine.

Despite, the fact that many of the outreach encounters were positive, and lead to participant enrollment, there were still several families who were not interested. The acceptance of preventative, and investigational, care is variable among families living in the same

community[1]. Many Amish families do not want to rely too heavily on "worldly knowledge".[1] In general, the head of the family makes healthcare decisions, thus healthcare usage varies among families in the same community.[1,36] When women were approached about the Research Registry, several expressed an interest in joining the registry but said they had to speak with their husbands; the brochure was a good resource to provide these women to share. Ultimately a "No" came back after their husbands were consulted. This finding supports the traditional Amish and Mennonite family structure and decision making. The research team members responsible for consenting families were female and found it much easier to connect with the Amish and Mennonite Woman compared to the men. This finding is supported by the gender hierarchy of their society. After speaking with several families who had declined participation in the research registry, a common response was noted, "humans can't know everything", which is consistent with the aforementioned philosophy.

The Amish and Mennonite have a strong devotion to community and making decisions based on the community's best interests.[1,36] When recruiting potential participants, the altruistic benefits of research enrollment, such as improving care delivery in communities, were presented. However, improvements may be needed in this information is presented because when discussing the registry with the potential participants and their families, they did not mention an interest in the community benefits or the need to discuss the information with members outside their family unit. Community minded decision making is complex and there is a need to continue to understand the nature of this decision making and how to improve our communication on community benefits.[1,36]

The research team had previously identified an Amish index family diagnosed with the first recorded mitochondrial respiratory chain defect in this population. A distant family member

was identified while being seen as an inpatient and was approached about the research registry opportunity. The family was extremely excited to see the research team. Upon entering the hospital room the family said, “someone who knows what we are talking about”, which was referencing their unique genetic health condition. It was wonderful and re-enforcing of the research efforts to see the family’s continued interest in medical research. The Plain Communities in other states and areas of Pennsylvania have been known to continue to participate in research.[3] They hope that better knowledge of disease affecting their communities will result in better treatment and reduced suffering. [3] The registry brochure was given to the patient and family to provide to other family and community members. Not long after consenting this index family the research team received a phone call from one of the family’s extended relatives who expressed an interest in joining the research registry after learning about it through their family.

The Medical Genetics division at this institution has several Amish and Mennonite research initiatives, which resulted in recruitment overlap. On several occasions, a potential participant would choose to participate in the research registry but would decline other research studies, such as the Whole Exome Sequencing in the Plain Communities project. It is notable that the registry did not require collection of blood or other samples, and declining other research often accompanied a statement such as “we don’t want to put him through anything else right now, he’s been through a lot”.

Lack of familiarity with the institution’s programs could impact a decision to participate in the registry. Discomfort with research that is genetic in nature could also impact decisions to participate, although qualitative research has shown Plain Community members have a general interest in understanding genetic conditions affecting their families.[37] When recruiting for the

research registry, potential participants were informed that not all possible future research is genetic, such as natural history studies or clinical drug trials. Limited experience in a medical and research center could also impact participation decisions. Reasons why community members say “no” to the research registry were not recorded, however, this would be interesting to explore in the future.

It was encouraging to see that the recruitment methods were well received in the community. The recruitment approach for the research registry was unique compared to research being done through other clinics and institutions. For example, the Clinic for Special Children in Strasburg, PA began as a primary care clinic, which spread by word of mouth through the Plain Community as a trusted resource for healthcare. After the primary care element of the Clinic for Special Children was established, research became available to community members. Patients being seen for primary care could be approached about research opportunities. Approach of research participants was likely easier because of the access to patients and the relationships and reputation the clinic had already developed within the community. Children’s Hospital of Pittsburgh of UPMC does not offer primary care services for this community. Successful recruitment to the registry can provide a model to other research teams with a limited relationship with the Plain Community.

3.4.3 Registry Development Limitations

Despite having IRB approval to recruit Amish and Mennonite patients at multiple hospitals under our institutional umbrella, with the exception of several participants recruited at the Medical Genetics Outreach Clinic at UPMC Horizon, researchers did not expand generally beyond the pediatric facility. The inpatient identification system only provided information for

patients within the Children's hospital. A grand rounds presentation on our Plain Communities program was provided for pediatric colleagues and to a group of primary care providers in one of the regional hospitals. Plans have been made to spread knowledge about the research registry to other hospitals and clinics in the UPMC network to improve recruitment across our healthcare system. The plan is to deliver similar presentations at other locations. Furthermore, our approach and recruitment was limited by the need to be selective in terms of which inpatient families were approached. For example, it would not have been appropriate to approach a family whose child was critically ill in the oncology unit. Team members tried to remain sensitive to a family's situation and priorities.

While challenging, recruitment through outreach to community leaders (bishops, deacons) will be attempted. There are many community leaders in western Pennsylvania, so this will be a slow process as familiarity with this community is developed. As relationships are built with the community, it will become easier to have input from the Plain Communities on research design and materials, such as the brochure. When developing a research project continued involvement of those research participants in the research process and design is important for creating a culturally safe space. [28] Due to the isolation of this population in Western Pennsylvania, it was not feasible to attempt this during the initial development process. For this reason, we asked for support and guidance from Dr. Holmes Morton was requested to ensure our recruitment approach was appropriate.

Although the team did not have access to a Pennsylvania Dutch interpreter, this was not expected to be a limitation for the recruitment process. All Amish and Mennonite learn English upon starting school and use English to interact with individuals outside the Plain Community.

The research team did not approach an Amish or Mennonite adult who did not speak English. The lack of an interpreter is not expected to hinder future recruitment.

It is not possible to provide statistical analysis on recruitment numbers because our recruitment size was not large enough to produce statistically significant data. Future directions include analyzing the effectiveness of using this community based registry for recruitment into future research studies.

3.5 CONCLUSIONS

Overall, the Research Registry was well accepted and the researchers anticipate continued recruitment and support from these communities. This Research Registry development provides the opportunity to enhance existing working relationships among the Amish, the Mennonites, and research communities in Western Pennsylvania. The idea for a community based research registry for vulnerable and underserved populations is not new. Previous vulnerable population research supports the idea that community research registries address disparities for access to and participation in research.[32,33] Despite the growing use of disease-specific research registries, there is a justification for community research registries because they have the potential to provide broader data for clinical outcomes, prevention, and epidemiology.[32,33] Successful development of this research registry may provide a model for other research institutions hoping to create positive and culturally sensitive research relationships with Amish and Mennonites in their communities.

4.0 RESEARCH SIGNIFICANCE TO GENETIC COUNSELING AND PUBLIC HEALTH

4.1 GENETIC COUNSELING SIGNIFICANCE

The development of an Amish and Mennonite Research Registry in western Pennsylvania holds importance to the field of genetic counseling because it provides an example of the unique roles genetic counselors hold within the research and public health fields. This project required many of the practice-based competencies included genetic counselor training[38]. This project required genetics expertise and analysis because of the unique genetic structure of the Amish and Mennonite populations[38]. It also required critical assessment of medical and social science literature to design the appropriate recruitment method[38]. Interpersonal, psychosocial and counseling skills were used extensively when recruiting potential participants[38]. These individuals were approached in the hospital setting, often with serious health concerns, requiring an empathetic conversation about medical and family histories. Genetic counseling training in eliciting a detailed pedigree was integral to the recruitment process[38]. This project also required appropriate education of potential participants with regards to what it means to be a part of a research registry as well as effectively educating families on the research process[38]. The project also required the development of appropriate patient educational materials, which is an important skillset of genetic counselors[38]. Lastly, this project drew heavily on the cultural competencies of

the genetic counselor. Genetic counselors are trained to recognize cultural differences and educate themselves on these differences in order to incorporate them into their work with patients[39]. It will be important to continue to have a genetic counselor integrally involved in the research registry.

Overall, the development of the research registry will add to the literature by providing a model for other research institutions who are hoping to develop a relationship with the Amish and Mennonite communities. It may provide a model for research recruitment in other vulnerable or underserved populations.

4.2 PUBLIC HEALTH SIGNIFICANCE: COMPETENCIES AND SERVICES

The core public health competencies are the skillsets of public health professionals. Many of these core competencies were used and developed throughout the project. These competencies included: analytical and assessment skills, communication, cultural competencies, community dimension of practice skills, public health science skills, and leadership and systems thinking skills[40]:

- *Analytical and assessment skills* encompass describing resources that can be used for improving the health of a community, assessing factors influencing health in a community, and making evidence based decisions. First, we described factors affecting the health of the Amish and Mennonite communities of western Pennsylvania and identified a need for a Research Registry that would improve access to health research in these communities. Several different platforms for data collection were assessed, and PhenoTips was chosen for data collection based on its ability to house the data elements

that were important to include for this population. Furthermore, in the development of the research registry, we paid careful attention to the ethical, legal, and social parameters important not only in gathering and storing patient information but also in approaching and consenting this population for research.

- *Communication* encompasses identifying the literacy of populations, communication with cultural proficiency, soliciting input from stakeholders, facilitating communication among groups, and disseminating public health data. We identified literacy level considerations for the Amish and Mennonite populations, incorporated cultural proficiency in written materials and conversations with community members, and facilitated communications among groups and organizations working with this population, such as the Mercer County Health Department and other Amish and Mennonite focused clinics. Additionally, we obtained input from Dr. Holmes Morton on our recruitment approach because of his trusted reputation within the Plain Community.
- *Cultural competencies* encompass describing diversity of individuals and communities, describing how diversity may influence programs and policies, and recognizing the benefits of diverse groups. We recognized how the Amish and Mennonite's unique culture may impact the health of the community and addressed this diversity in our recruitment and consenting approach. Through our research and interaction with the community we understood the limited interaction the Plain Communities of western Pennsylvania have with modern health care which could impact their understanding of health-related research. We used plain language in our conversations and in our written materials.

- *Community dimension of practice skills* encompass describing programs and services that improve health in a community and collaborating with community health partners. We identified existing services for the Amish and Mennonite communities, collaborated with community health partners such as the Mercer County Health Department, and identified a need for additional services within the community such as the Clinic for the Plain Communities.
- *Public Health Science skills* encompass describing the scientific foundation of public health, identifying events in public health, retrieving public health evidence and describing regulations for ethical research conduct. We conducted ethical research by choosing a registry and research design that would protect patient confidentiality and limit risks to this vulnerable population. We chose the PhenoTips database because it was HIPAA compliant, password protected, and downloaded behind the institutional firewall. The only risk associated with the research registry was breach of confidentiality but we developed many safe guards to limit this risk.
- *Leadership and systems thinking skills* encompass incorporating ethical standards of practice, describing public health as interconnected organizations, and identifying ways for these organizations to work together. We recognized the opportunity to collaborate with other institutions and organizations. We collaborated with Dr. Holmes Morton and the Consortium of Clinics serving the Amish and Mennonite communities as well as the Public Health community in Mercer County.

The 10 Essential Public Health Services are community activities for public health systems, which include: monitoring health, diagnosing and investigating health problems, educating

people about health, mobilizing community partnerships, develop policies, enforce laws and regulations, link people to serves to provide care, ensure a competent workforce, evaluate services, and research for new insights.[41] The development of the Amish and Mennonite Research Registry was a public health activity that used several of these public health foundations.

- *Inform, educate, and empower people about health issues*: We educated the Amish and Mennonite communities on medical research opportunities that may have the potential to improve their health and/or the general health of their communities.
- *Mobilize community partnerships to identify and solve health problems*: We collaborated with the Mercy County Health Department and with Dr. Holmes Morton to promote the Amish and Mennonite Research Registry and health improvement in the Plain Communities.
- *Research for new insights and innovative solutions to health problems*: We designed the Amish and Mennonite Research Registry to provide a platform for recruiting members of the Plain Community to future research studies. Future research will provide insight into the health of the Amish and Mennonite communities of western Pennsylvania.

5.0 PUBLIC HEALTH CHAPTER

5.1 AMISH BACKGROUND

The Amish of western Pennsylvania are genetically isolated religious communities that have an increased incidence of a number of autosomal recessive conditions resulting from genetic founder effects caused by their European migration in the 17th century, where a small group of people settled in Pennsylvania.[1–4] An autosomal recessive mutation will become more prevalent in an isolated population in successive generations of inbreeding.[3] The Amish, Mennonite and Hutterite Disorder Database focuses on single gene Mendelian disorders and mutations specifically identified in the Plain Communities[14]. The database has a record of close to 200 OMIM single gene Mendelian disorders.[14] There are also many new disorders being identified and described in these communities to date.

There are an estimated 308,000 Amish individuals living in 23 states in the United States today.[6] These Amish communities are isolated geographically and socially, and culturally limit their use of organized medicine unless necessary. This can be seen by providers as a barrier to healthcare delivery. Furthermore, these communities do not participate in traditional health insurance programs, which leaves many Amish families dealing with the financial burden of expensive medical bills or relying on Plain Community systems of financial support for healthcare coverage.[8,9] Public health efforts, such as improving access to care, improving access

to research opportunities, and minimizing healthcare costs are important for improving health disparities in this population.[10] These efforts will need to incorporate cultural differences into their design and materials; such as differences in education, language, decision making styles, religion, and perception of modern medicine.

As part of the development of the Amish and Mennonite Research Registry, a brochure was written to inform participants of what it means to be a part of a research registry. The Amish population has limited knowledge of research registries, but also may have limited experience with modern healthcare. When constructing this brochure, we took into consideration the specific cultural differences of this population in addition to education level and health literacy.

5.2 GENERAL HEALTH LITERACY

5.2.1 What is Health Literacy?

The Center for Disease Control and Prevention (CDC) defines health literacy as "skills people use to realize their potential in health situations. They apply these skills either to make sense of health information and services or provide health information and services to others".[42] Health literacy skills are needed to find health related services, communicate health needs, process health information provided by healthcare providers, and to understand the benefits, risks, and limitations of health choices.[42] Health literacy skills include numeracy skills, basic literacy skills, and previous medical or health information knowledge.[42] A national assessment of health literacy revealed that only 12% of all adults in the United States are proficient in health literacy.[43] The US Department of Education and National Institute of Literacy report that 21% of

adults in the United States read below the fifth grade and 14% of all adults cannot read.[43] Health literacy is different from general literacy. An individual can have a high or average literacy level but below average health literacy level, however they may be related.[42–44] Certain populations have a higher incidence of low health literacy, such as older adults, minority groups, those who speak English as a second language, those with low educational attainment, and people with low incomes.[45] Many of these risk factors apply to the Amish population.

5.2.2 Health Literacy and Health Outcomes

Low health literacy has been associated with poor health outcomes. Research shows that individuals with low health literacy present themselves for care when they are sicker and have an increased rate of hospital and emergency service use.[44] These individuals are also less able to manage chronic health conditions, such as diabetes.[46] They have limited knowledge of their chronic condition and they lack the health literacy skillset to manage a complex condition. Those with low health literacy do not seek out preventative healthcare, such as mammograms, as often as those with higher health literacy.[44] Martin et al, studied the relationship between health literacy and patient self-advocacy.[47] The researchers assessed whether reading, numeracy, speaking, and listening were associated with self-advocacy when scheduling a medical appointment when a barrier exists. Researchers recruited 914 participants, in their mid-forties, from the New England Family Study. Participants were given a scenario about an individual named Joe who was told it would be a month until the next available appointment and were then asked what Joe should do. Participants with better speaking and listening skills were associated with better patient advocacy or proactive responses to Joe's problem. The research revealed that patients with higher health literacy were more assertive, willing to challenge health care

providers, and participate in decision-making, compared to those patients with lower health literacy.[47] Research studies have also shown a relationship between health literacy, health outcomes, and health costs. Those with higher activation, defined as knowledge, skill and confidence to manage one's health, tend to have higher health literacy.[48] Hibbard and Greene found that higher patient activation is associated with better health outcomes and lower health care costs through their review of several health outcome studies.[48] One study by Hibbard et al, assessed patient activation and health outcomes.[49] This was a cross-sectional study of 25,047 adult patients at Fairview Health Services in Minnesota. Patient activation was measured using the Patient Activation Measure (PAM), which measures one's confidence and skills for managing health related tasks. Researchers assessed four outcome areas: prevention, unhealthy behaviors, clinical indication, and costly utilization. Electronic medical records were reviewed for health outcome data. Participants with lower activation had higher costly utilization, such as emergency room visits, and utilized fewer preventative health services. Data suggest a higher health care costs for those with lower patient activation. [49]

5.2.3 Incorporating and Measuring Health Literacy

Public Health professionals are responsible for making sure programs and communication incorporate health literacy. There are a variety of resources available to public health professionals to help meet these goals, which include laws, guidelines, standards, and literacy assessment tools.

The use of plain language is integral to improving health literacy. Plain language is communication that is easy to understand the first time. In 2010 the Plain Language Act was passed requiring all federal agencies to be trained in plain language practice.[50,51] The purpose of

this Act was to improve accountability of Federal agencies to the public for communication that the public can understand.[50] This act lead to the development of Federal Plain Language Guidelines that are accessible to all public health professionals providing advice for clear communication.[50] In addition, the government has developed other standards for professionals and organizations including Linguistically Appropriate Services Standards.[51] These cultural linguistic competencies require a public health professional to recognize that culture affects communication and the context of that communication.[51] These standards provide professionals with standards for addressing differences in culture and language that may affect health literacy.[51]

Measuring health literacy is an important component of program and material development. It can sometimes be difficult to measure health literacy because there are multiple health literacy skills that need to be assessed and previous health experiences can impact an individual's interpretation and understanding of health information.[44] Despite the challenges of assessing health literacy, there are tools available to aid organizations, researchers, and healthcare professionals with general assessments of health literacy. For Example, the Agency for Healthcare Research and Quality (AHQR) developed the Rapid Estimate of Adult Literacy in Medicine (REALM), which is a 60-item word recognition test that provides a health care professional a quick assessment of patient or participant literacy.[51] Those that score less than six are considered at risk for poor health literacy. [51]

There are several programs that assess the reading level of written materials. However, the US Department of Health and Human Services cautions that these readability formulas should not be used alone to assess the ease of reading because important factors are ignored in these formulas.[52,53] For example, these tools may calculate a low reading level but written

material may not be clear or effective.[52,53] Considering factors such as attracting and holding reader attention and creating a material that looks easy to read as to not scare a reader away, are important for creating clear, effective materials. Other limitations include caveats such as, a long word being more familiar than a shorter alternative, use of a long word that is important but that needs to be defined, or the potential for creating many shorter sentences from a longer sentence which may in turn affect the flow and readability of a text.[52,53] It is recommended that readability formulas be used to indicate the general range of difficulty because they are not 100% accurate or precise.[52] For example, a text that is scored by two different people may result in different grade level scores. This can occur because formatting such as headings, bullet points, and mid-sentence punctuation can affect the way the readability formula scores the text.[52,53]

5.3 AMISH HEALTH LITERACY

Literacy level and English as a second language are important considerations when developing written materials for the Amish. The Amish speak Pennsylvania Dutch, a derivative of German, until they begin school and learn English.[1] However, they continue to rely on Pennsylvania Dutch in their own communities. Children in the Amish community will attend school from grade one to grade eight and then they begin full time work, usually on the family homestead.[1] The Amish build and staff their own schools. School boards consisting of parents and members of the local church manage these schools.[1] Most lessons are taught orally and by example, typically by uncertified teachers from within the community.[1] Curriculum varies depending on state requirements, however, few schools teach about health and the sciences. Many community schools have difficulty finding English reading material that respects their

religious and community views.[1] Additionally, the Amish lifestyle restricts television, radio, and computers, limiting possible interactions with English learning outside the classroom.[1]

Health literacy levels in the Amish do have the potential to affect health status and health outcomes. Although the Amish have low incidences of cancer, they have a high rate of advanced staged disease and low screening rates when compared to the general population.[54,55] Katz et al., assessed the screening practices among Amish and non-Amish adults living in Ohio.[55] The researchers conducted face-to-face interviews with 134 Amish and 154 non-Amish participants. Interview questions pertained to perception of risk, cancer screening behaviors, and screening barriers.[55] Researchers found that the Amish had lower rates of cancer screening, which may be attributed to geographical isolation, transportation limitations, lack of health insurance, and lack of knowledge regarding preventative health care.[55] Health literacy may be one factor impacting these findings and other healthcare outcome data.[54] Research in the general population has shown that individuals with lower health literacy present for care when they are sicker and do not seek preventative health care services as often as those with higher health literacy levels.[44] Cultural differences and differences in health practices also need to be recognized as a barrier to healthcare access and a factor impacting health literacy levels in the Amish.[56]

A study by Katz et al., compared health literacy in Amish and non-Amish living in the Ohio Appalachian region.[54] These researchers use the Rapid Estimate of Adult Literacy in Medicine (REALM) tool, via a mailed survey, to assess health literacy levels. The REALM scores were significantly lower in Amish males and females than in the non-Amish control groups. Results showed that 12% of Amish participants had lower than a 6th grade reading level, compared to the 2.6% in the non-Amish participant group. The researchers suggest that the unique Amish culture could be contributing to the health literacy differences because health

literacy involved not only reading and writing abilities but cultural and conceptual knowledge, oral literacy, numeracy, and media literacy. The Amish remain socially isolated creating a different cultural context for health information. The results do indicate a need for unique strategies when communicating health information to the Amish and materials should be written below the eighth-grade reading level. There has been limited research on health literacy in the Amish and there is a need for a better understanding to parse out some of the complex factors affecting health literacy and health outcomes, such as cultural context and English as a second language.

5.4 ASSESSMENT OF THE RESEARCH REGISTRY BROCHURE AND OUTSIDE AMISH MATERIALS

5.4.1 Methods

5.4.1.1 Research Registry Brochure Development

The Research Registry brochure was designed to provide participants with information on what it means to be a part of a Research Registry. It was also designed as a resource to pass along to spouses, family, and community members. The aim when designing the brochure was to keep sentence structure simple and the literacy level at the eighth-grade or below. The title of the brochure was “What does it mean to be part of a research registry?”. Topics covered in the brochure included the purpose of the registry, benefits of participation, what is required of a

participant, who is eligible, privacy, cost, compensation, and study withdrawal. The full brochure can be found in Appendix D.

The Research Registry brochure was designed with several factors in mind including readability scores, reader's knowledge and perspectives, layout, style, and cultural appropriateness. When designing materials, it is important to adopt the perspective of the reader. The reader has limited knowledge of the subject and so the purpose of the material needs to be clear and effective.[52] The Amish population has limited knowledge of research registries, but also may have limited experience with modern healthcare.[1] It is also important to attract the reader and retain their interest in the material. The Amish and Mennonite Research Registry brochure was written to inform participants of what it means to be a part of a research registry. Readers spend minimal time on materials and so it is important to provide the most important information succinctly.[52] The Research Registry brochure was limited to two pages of the most important information from the consent form, with the intent to make the brochure appear manageable to read. The design of the Research Registry brochure was uncluttered, incorporated white spaces, and an obvious path for the reader to follow, helping with ease of reading[52]. Headings were used to emphasize important topics.[52] Researchers also pulled out short phrases from the text, such as "All participation is voluntary and confidential" to emphasize important points.[52] Materials should be written in an active and conversational style, which researchers tried to achieve with the registry brochure.[52] Researchers also made sure the Research Registry brochure content was culturally appropriate. Images of humans were avoided because many Amish and Mennonites avoid personal photographs.[1] Farming and simple country scenes are familiar to the Plain Communities; therefore, a single image of a farm and flowers was chosen for the front cover. The Amish and Mennonites are family and community oriented; therefore,

family and community members were referenced in the brochure. A simple, culturally appropriate color scheme was also chosen.[1,36]

5.4.1.2 Outside Amish Materials

Other research registry educational materials designed for the Amish were not available for comparison. Furthermore, it was difficult to locate educational materials designed with the Amish community in mind. Researchers assessed a flyer informing Amish parents about Rh disease as well as a newsletter written by the Community Health Clinic. These two materials were chosen because they were accessible to the research team. The flyer on Rh disease was written to inform mothers in the Plain Communities about Rh blood type testing and the Rh immunoglobulin injection to prevent Rh disease in a new baby. The flyer was designed by the clinic staff at the Clinic for the Plain Communities for an Amish Safety day in Mercer County. The flyer was titled “What is Rh disease and how can it affect my baby?”. It covered what Rh disease is, how it affects a pregnancy, and prevention. The Community Health Clinic distributes a regular newsletter to Plain Community members, financial supporters of the clinic, and others they collaborate with, such as the Children’s Hospital of Pittsburgh of UPMC. Topics covered in the newsletter were broad and included clinical research opportunities, fundraising events, and patient care initiatives.

5.4.1.3 Material Evaluation

The Coleman-Liau online readability formula was used to assess the general readability of the documents. The Coleman-Liau scoring method factors in the number of characters in a word instead of the most traditional syllable count.[52] This is thought to be a more accurate method for computer readability programs.[52]

Although the US Department of Health and Human Services cautions that readability formulas not be used alone to assess the ease of reading, the Coleman-Liau Readability score was used to assess the general difficulty of the brochure.[52,53] The US Department of Health and Human Services recommends scoring the readability of materials by hand using either the FRY or SMOG methods. However, because the Research Registry brochure text was short, the FRY and SMOG methods were not an option.[52] FRY requires three 100-word passages consisting of sentences for scoring and SMOG requires 30 consecutive sentences in a single block or a sample of 10.[52] For the purpose of consistency, researchers used the same readability formula for the Rh disease flyer and The Community Health Clinic newsletter. The CDC rates the 7-8th grade reading levels as average difficulty and a readability target for material geared toward the general public. The 4-6th grade reading levels are rated as easy.

The Center for Medicaid and Medicare services, under the U.S. Department of Health and Human Services, houses a "Toolkit for making written material clear and effective".[52] This toolkit consists of a series of 11 tutorials designed to provide guidance on the following topics: using a reader centered approach, guidelines for writing, guidelines for design, using readability formulas, material for older adults, material for the web, and guidelines for translation. The tutorials on using a reader centered approach, guidelines for writing, guidelines for design and using readability formulas were referenced during the development of the Research Registry Brochure. This tool kit was also used to assess the general design of the Rh disease flyer and The Community Health Clinic newsletter.

Post brochure design, a CDC Clear Communication Index Score Sheet was identified.[57] It was used to assess the brochure for this public health chapter and for future brochure improvements. It assesses the main message, language used, information, design, behavioral

recommendations, use of numbers, and risk communication[57]. Behavioral recommendations, use of numbers, and risk communication did not apply to the Research Registry brochure or the Rh disease flyer, however, the index score sheet was still used to assess the main message, language, and design. The CDC score sheet was not used to score the newsletter because the message was too broad and did not encompass a single topic.

5.4.2 Results

The Research Registry brochure was assessed using the Coleman-Liau readability score. The Research Registry brochure scored a 7.8 on the Coleman-Liau readability scale, which correlates roughly to a 7th grade reading level. The CDC rates the 7-8th grade reading levels as average difficulty and a readability target for material geared toward the general public. Since the Coleman-Liau readability formula does not account for the number of syllables in a word, a list of difficult words, defined as three or more syllables, are include in Table 1. Using the CDC Communication Index Score Sheet, the brochure scored a 9 out of 11, or 81.8%. The brochure lost points for not having a visual cue that conveys the message and for not having a call to action. These results are summarized in Table 2.

The flyer on Rh disease, targeted toward the Plain Communities, was assessed using the Coleman-Laui readability scale. The content of the flyer scored a 9.8 on the Coleman-Liau readability scale. This indicates that the reading level of the flyer is at the 9th grade reading level. Since the Coleman-Liau readability formula does not account for the number of syllables in a word, a list of difficult words, defined as three or more syllables, are included in Table 1. Using the CDC Communication Index Score sheet, the flyer scored an 8 out of 11, or 72.7%. The flyer

lost points for not having a visual that conveys the message, for not having information in bullet format, and for not stating the author of the material. These results are summarized in Table 2.

The Community Health Clinic newsletter scored a 13.2 on the Coleman-Liau readability scale. This indicates that the reading level of the newsletter was at a college level. Since the Coleman-Liau readability formula does not account for the number of syllables in a word, a list of difficult words, defined as three or more syllables, are included in Table 1.

Table 1. Evaluation of written Amish materials

Amish Material	Coleman-Liau Readability Score	Number of pages	List of difficult words (greater than three syllables)
Research Registry Brochure	7.8	2	Registry Mennonite Participate/Participation Advocate Hesitate Community Interested Appropriate Medical Increasing Voluntary Confidential Permission Protected Relationships
Rh Disease Flyer	9.8	1	Antibodies Sensitization Jaundice Bloodstream Anemia Immunoglobin Phototherapy Transfusion
Community Health Clinic Newsletter	13.2	12	Examples: Qualified Accurate Eliminating Attendees Misdiagnosed

Table 2. CDC Communication Index Score categories used for assessment[57]

Main Category	Questions	Score (No=-1)
Main Message and Call to Action	Does the material contain one main message?	
	Is the main message at the top, beginning, or front of the material?	
	Is the main message emphasized with visual cues?	
	Does the material contain at least one visual that conveys or supports the main message?	Brochure -1 Flyer -1
	Does the material include one or more calls to action for the primary audience?	
Language	Do both the main message and the call to action use the active voice	Brochure -1
	Does the material always use words the primary audience uses?	
Information Design	Does the material use bulleted or numbered lists?	Flyer -1
	Is the material organized in chunks with headings?	
	Is the most important information the primary audience needs summarized in the first paragraph or section?	
State of the Science	Does the material explain what authoritative sources, such as subject matter experts and agency spokesperson, know and don't know about the topic?	Flyer -1

5.4.3 Discussion

The CDC rates the 4-6th grade reading levels as easy to read and the 7-8th grade reading level as average reading difficulty and a readability target for material geared toward the general public. The materials assessed scored a 7th grade reading level and above. This is concerning considering that Katz et al. found that a significant portion of the Amish population in Ohio

(12%) had a literacy level less than the 6th grade.[54] This is compounded by the fact that the target population only attends school to the 8th grade and speaks English as a second language.[1] Given the average education level of the Amish population, it would be more effective if materials were written at a 4th-6th grade reading level. This could have been achieved by substituting complex words within the document for simpler ones.

The materials contained many words that could have been substituted for more clear or concise ones. For example, in the brochure the word "confidential" was used when instead a shorter more common word such as "private" would have been more appropriate in this context. The materials contained longer words which would have increased the overall readability score of the document. It is important to note that several longer words, such as "Mennonite" found in the brochure, would be understandable and known to the Amish community. Alternatively, there were shorter words that would have passed as readable when run through a readability formula but may not be suitable for the intended audience. For example, "gene" was used in the newsletter but may be a concept only those with a science background would understand. There are exceptions to the suggested length of words used in public health materials, such as longer words that are familiar are okay to use, which is why readability formulas cannot be used alone to assess the ease of reading of a document and instead should be used to assess general readability. [52,53]

It is important to maintain consistency throughout patient educational material as inconsistency can confuse readers. The Rh disease flyer was inconsistent in defining technical and medical words. Medical terms such as "blood transfusion" were not defined in the document. Given the isolation of the Amish community, many individuals may not be familiar with this common terminology. However, the flyer defined some medical terms and these

definitions were written in plain language. Examples included jaundice and phototherapy. The term jaundice was defined as “yellowing of the skin and eyes”. In the researcher’s assessment, the flyer would have been comprehensive without using medical terminology. The integrity of the message would not have been compromised if the writers had only written “yellowing of the skin and eyes”. Sand-Jeddin et al. studied the impact of medical terminology on the readability of health educational materials. [58] They analyzed five health educational brochures with the SMOG and FRY readability formulas.[58] They first assessed readability of the documents with medical terminology included in the text, followed by an assessment of the readability with medical terminology removed from the text.[58] Reading levels were significantly lower after removal of medical terminology.[58] Materials should focus on the patient experience, not medical terminology, otherwise patient understanding is compromised. [59] One way to improve the reading level of the materials assessed in this study would be to remove medical terminology, which would not affect the integrity of the message.

The CDC index score sheet recommends improving materials that score below 89%, which suggests that both the brochure and the flyer should be revised considering the score of 81.8% and 72.7% respectively. The index scoring sheet suggests that these materials could be revised to include a visual cue that pertains to the main message. However, when designing the brochure, the need for visual cues was limited based on the nature of the content. The creators of the Rh disease flyer were likely limited in images they could choose because the Amish prefer not to have photos taken of themselves.[1] It is recommended when developing educational materials that the author include illustrations to draw the reader’s attention and to aid in understanding of the main message.[52] However, for this population given the avoidance of human photographs and preferences for simple materials, this suggestion may not be appropriate.

The index scoring sheet also suggests the brochure should be revised to include a call to action, however, the purpose of the brochure was not to change a health behavior but to educate potential participants about the intent of a research registry. It is the opinion of the researchers that the Rh disease flyer be revised to incorporate bulleted lists, instead of having information in paragraph form, and to include the authors of the information so that readers know it is from a trusted source. Overall, the CDC Communication Index Score Sheet is a guide for the designer to reflect on content and design and not a precise tool, therefore, there will be exceptions for scoring.[57]

The Rh disease flyer and The Community Health Clinic newsletter were assessed using the U.S. Department of Health and Human Services "Toolkit for making written material clear and effective" for general design and layout. The Rh disease flyer was well designed based on suggestions outlined in the toolkit. It contained headings to highlight important topics. Additionally, the document was one page and incorporated white spaces, as to not overwhelm the reader with text, which is relevant to the assessment given that readers spend minimal time on materials, and so it is important to provide the most important information succinctly.[52] Illustrations used in the flyer were culturally appropriate. The flyer had two images of quilts, likely made by the Amish community, which is in keeping with the Amish preference to avoid photographs of humans.[1] Unlike the Rh disease flyer, the Community Health Clinic newsletter did not incorporate many of the criteria outlined in the U.S. Department of Health and Human Services Toolkit. The newsletter contained few images to break up the amount of space used for written content. Furthermore, there was little white space and few section headings to break up the words on a page. This does not provide the reader with the impression of a manageable read. Readers tend to skim material when it is in large text blocks and this could affect their

understanding.[52] The number of pages was not factored into the assessment because of the nature of the document; newsletters are expected to be longer than educational brochures and flyers. One strength of the newsletter is that images chosen for the newsletter were culturally appropriate, again avoiding the use of human images, and the color scheme and layout were not "flashy", which is in keeping with the Amish preference for simplicity.[1] Given the cultural appropriateness of the flyer and newsletter, the materials were effective for their target population and served their intended purpose.

5.4.4 Conclusions

It is difficult to compare the Research Registry brochure, the Rh disease flyer, and The Community Health Clinic newsletter because they were created with very different purposes in mind. However, general readability and cultural sensitivity are important for any document designed for the Amish community. The materials assessed scored a 7th grade reading level and above, which is concerning for this population given factors such education level and English as a second language.[1] Greater effort should have been made to simplify word choices, language, and definitions. The creators of these documents were mindful when it came to the cultural appropriateness of image choices and color schemes. When designing materials for the Amish population, authors should use the readability assessment tools available to public health professionals to gage the general readability and design of their materials. Health literacy is an important element for disseminating public health information.

APPENDIX A: IRB APPROVAL LETTER

University of Pittsburgh
Institutional Review Board

3500 Fifth Avenue
Ground Level
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
http://www.irb.pitt.edu

Memorandum

To: Lina Ghaloul Gonzalez
From: IRB Office
Date: 11/15/2016
IRB#: MOD16030311-01 / PRO16030311
Subject: Amish/Mennonite Registry

The University of Pittsburgh Institutional Review Board reviewed and approved the requested modifications by expedited review procedure authorized under 45 CFR 46.110 and 21 CFR 56.110.

Modification Approval Date: 11/15/2016
Expiration Date: 9/27/2017

For studies being conducted in UPMC facilities, no clinical activities that are impacted by the modifications can be undertaken by investigators until they have received approval from the UPMC Fiscal Review Office.

Please note that it is the investigator's responsibility to report to the IRB any unanticipated problems involving risks to subjects or others [see 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)]. Refer to the IRB Policy and Procedure Manual regarding the reporting requirements for unanticipated problems which include, but are not limited to, adverse events. If you have any questions about this process, please contact the Adverse Events Coordinator at 412-383-1480.

The protocol and consent forms, along with a brief progress report must be resubmitted at least one month prior to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh), FWA00003567 (Magee-Womens Health Corporation), FWA00003338 (University of Pittsburgh Medical Center Cancer Institute).

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

APPENDIX B: PARTICIPANT CONSENT FORMS

B.1 ADULT CONSENT FORM

CONSENT FOR AN ADULT TO ACT AS A PARTICIPANT IN A RESEARCH REGISTRY

TITLE: Amish/Mennonite Registry

PRINCIPAL INVESTIGATOR: Lina Ghaloul Gonzalez, M.D.
Research Assistant Professor, Medical Genetics

CO-INVESTIGATORS: Gerard Vockley, MD, PhD
Amy Goldstein, MD
Catherin Walsh Vockley, MS, LCGC
Christine Munro, B.Sc

SOURCE OF SUPPORT: Division discretionary funds

What is the purpose of this research?

A great deal of medical knowledge has come from people volunteering to be part of clinical research. The goal of this study is to make a registry, or a list, of people from the Plain Community who want to help with medical research. A registry makes it easier to contact and let people know about studies that might be right for them. Researchers sometimes decide to contact a person for a study by looking at their medical record information. We are asking permission to add your name to the registry of Plain Community members who may want to take part in medical research. We are also asking to collect and store your medical record information in an

Amish/Mennonite Registry. Creating a registry will help researchers plan studies that help us understand diseases that commonly affect people of the Plain Community.

The Research Registry will help our investigators in two important ways.

1. It will help researchers find patients who could be offered a place in future research studies. For example, physicians and other researchers from Children's Hospital of Pittsburgh work on studies for undiagnosed diseases, population genetics, and treatment safety. If you agree to be part of this Research Registry, your medical record information may be looked at by doctors and researchers to see if you are a good fit for a future research study.

2. It could help researchers to look at the medical records of many people to answer questions about a disease and its treatment.

Who is being asked to participate in this Research Registry?

Men, women, and children from the Amish and Mennonite communities are being asked to participate in this Research Registry.

What will my participation in this Research Registry involve?

If you agree to join the Amish/Mennonite Research Registry, you will be asked to sign this document. Signing will let us collect and store your medical records in the registry. The medical information to be collected will include: age, past medical history, future diagnoses, diagnostic procedures, test results, including genetic tests. You will be asked about your family's medical history in order to make a family pedigree, or tree. This family tree will also be stored in the registry. We are asking that you let us contact you if a researcher decides that you are a good fit for a future research study. If you are contacted about a future study, you will be given

information about the new study. If you then choose to join the study, you will be asked to sign a new consent form for that study. You may also choose not to join the new study.

What are the possible risks of my participation in the Research Registry?

There are no risks of physical injury with your participation in the Amish/Mennonite Research Registry, however, this Research Registry does involve the possible risk that information about your health might become known to people outside of the Children's Hospital of Pittsburgh of UPMC.

We will make every effort to keep your medical records private by storing them in a safe place. All information will be stored in locked, limited-access settings. Access to information within the Research Registry will only be given to researchers with permission from the registry team.

What are the possible benefits of my participation in the Research Registry?

This Research Registry will be used to contact you for future research studies in the Plain Community. Joining a future research study could have a positive affect on your medical care, as well as the general care in your community.

Will I or my insurance provider be charged for my participation in the Research Registry?

There will be no costs to you or your insurance provider to participate in this Research Registry.

Will I be paid for my participation in the Research Registry?

No, you will not receive any payment for participating in this Research Registry.

Who will know about my participation in this Research Registry?

We will not tell anyone that you are part of the Research Registry without your permission. Any information from your medical records that is put into this Research Registry will be kept private. Also, your name will not be in any information unless you sign another form (release) giving your permission to share information.

Who will have access to my identifiable medical record information contained in the Research Registry?

Access to your medical record information in the Research Registry will only be given to the registry team and other researchers given access by the registry team for use in future research studies. All access will be carefully controlled by the registry team.

In addition, the following people may have access to your medical record information in this Research Registry:

Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may look at information in the Research Registry to make sure that your privacy is being taken care of correctly.

In unusual cases, the researchers may be required to release your medical record information from the Research Registry because of a court order.

For how long will my medical record information continue to be placed in the Research Registry and for how long will this information be used for research purposes?

We will keep and use your medical record information in the Research Registry for an indefinite period of time or until you let us know in writing that you want to leave the Research Registry.

Is my participation in the Research Registry voluntary?

Joining the Amish/Mennonite Research Registry is completely voluntary. Whether or not you choose to join this Research Registry will have no effect on your current or future medical care at the University of Pittsburgh Medical Center or other health care providers, and it will not affect your relationship with a health insurance provider or the University of Pittsburgh.

May I withdraw, at a future date, my consent for participation in this Research Registry?

You may leave the Amish/Mennonite Research Regstry at any time. To formally leave the Amish/Mennonite Research Registry, you should send a written and dated letter of your decision to leave the Research Registry. The address can be found on the first page of this consent form.

VOLUNTARY CONSENT

All of the above has been explained to me and all of my current questions have been answered. I understand that I should ask questions about any part of my participation in the Amish Mennonite Research Registry at any time. Future questions will be answered by the coordinators of the registry. I understand that a copy of this consent form will be given to me.

I understand that any questions I have about my rights as a participant in the Research Registry will -be answered by the Human Subject Advocate of the IRB office, University of Pittsburgh (1-866-212-2668).

By signing below, I agree to participate in the Amish/Mennonite Research Registry and provide my permission to share my medical records with the research team.

_____ _____

Participant's Signature Date

The participant is unable to consent because: _____

I certify that under state law I am the parent/guardian or legally authorized representative (LAR) of the participant named above and that I am authorized to sign this consent to his/her participation in the research study and provide my authorization to share his/her medical records with the study team described above. I am also authorized to allow the use and sharing of the participant's study-related records as described above.

_____ _____

Name of Parent/Guardian or LAR (Print) Relationship (Print)

_____ _____

Signature of Parent/Guardian or LAR Date

_____ _____

Witness Signature Date

CERTIFICATION OF INFORMED CONSENT

I certify that I have explained the nature and purpose of the Amish Mennonite Research Registry to the above-named individual, and I have discussed the possible risks and potential benefits of participation in this Research Registry. Any questions the individual has about this Research Registry have been answered, and the physicians and research staff associated with the Amish Mennonite Research Registry will be available to address future questions as they arise.

_____

Printed Name of Person Obtaining Consent

_____ _____

Signature of Person Obtaining Consent Date

B.1 CHILD CONSENT FORM

CONSENT FOR A CHILD TO ACT AS A PARTICIPANT IN A RESEARCH REGISTRY

TITLE: Amish/Mennonite Registry

PRINCIPAL INVESTIGATOR: Lina Ghaloul Gonzalez, M.D.
Research Assistant Professor, Medical Genetics

CO-INVESTIGATORS: Gerard Vockley, MD, PhD
Amy Goldstein, MD
Catherin Walsh Vockley, MS, LCGC
Christine Munro, B.Sc

SOURCE OF SUPPORT: Division discretionary funds

What is the purpose of this research?

A great deal of medical knowledge has come from people volunteering to be part of clinical research. The goal of this study is to make a registry, or a list, of people from the Plain Community who want to help with medical research. A registry makes it easier to contact and let people know about studies that might be right for them. Researchers sometimes decide to contact a person for a study by looking at their medical record information. We are asking permission to add your child's name to the registry of Plain Community members who may want to take part in medical research. We are also asking to collect and store your child's medical record information in an Amish/Mennonite Registry. Creating a registry will help researchers plan studies that help us understand diseases that commonly affect people of the Plain Community.

The Research Registry will help our investigators in two important ways.

1. It will help researchers find patients who could be offered a place in future research studies. For example, physicians and other researchers from Children's Hospital of Pittsburgh work on

studies for undiagnosed diseases, population genetics, and treatment safety. If you agree to have your child participate in this Research Registry, their medical record information may be looked at by doctors and researchers to see if they are a good fit for a future research study.

2. It could help researchers to look at the medical records of many people to answer questions about a disease and its treatment.

Who is being asked to participate in this Research Registry?

Men, women, and children from the Amish and Mennonite communities are being asked to participate in this Research Registry.

What will my child's participation in this Research Registry involve?

If you agree to allow your child to join the Amish/Mennonite Research Registry, you will be asked to sign this document. Signing will let us collect and store your child's medical records in the registry. The medical record information to be collected will include: age, past medical history, future diagnoses, diagnositic tests, test results, including genetic tests. You will be asked about your family's medical history in order to make a family pedigree, or tree. This family tree will also be stored in the registry. We are asking that you let us contact you if a researcher decides that your child is a good fit for a future research study. If you are contacted about a future study, you will be given information about the new study. If you then choose to allow your child to join the study, you will be asked to sign a new consent form for that study. You may also choose not to join the new study.

What are the possible risks of my child's participation in the Research Registry?

There are no risks of physical injury with your child's participation in the Amish/Mennonite Research Registry, however, this Research Registry does involve the possible risk that

information about your child's health might become known to people outside of the Children's Hospital of Pittsburgh of UPMC.

We will make every effort to keep your child's medical records private by storing them in a safe place. All information will be stored in locked, limited-access settings. Access to information within the Research Registry will only be given to researchers with permission from the registry team.

What are the possible benefits of my child's participation in the Research Registry?

This Research Registry will be used to contact your child for future research studies in the Plain Community. Joining a future research study could have a positive affect on your child's medical care, as well as the general care in your community.

Will I or my child's insurance provider be charged for my participation in the Research Registry?

There will be no costs to you or your child's insurance provider to participate in this Research Registry.

Will I be paid for my child's participation in the Research Registry?

No, your child will not receive any payment for participating in this Research Registry.

Who will know about my child's participation in this Research Registry?

We will not tell anyone that your child is part of the Research Registry without your permission. Any information from your child's medical records that is put into this Research Registry will be kept private. Also, your child's name will not be in any information unless you sign another form (release) giving your permission to share information.

Who will have access to my child's identifiable medical record information contained in the Research Registry?

Access to your child's medical record information in the Research Registry will only be given to the registry team and other researchers given access by the registry team for use in future research studies. All access will be carefully controlled by the registry team.

In addition, the following people may have access to your child's medical record information in this Research Registry:

Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may look at information in the Research Registry to make sure that your child's privacy is being taken care of correctly.

In unusual cases, the researchers may be required to release your child's medical record information from the Research Registry because of a court order.

For how long will my child's medical record information continue to be placed in the Research Registry and for how long will this information be used for research purposes?

We will keep and use your child's medical record information in the Research Registry for an indefinite period of time or until you let us know in writing that you want to leave the Research Registry.

Is my child's participation in the Research Registry voluntary?

Joining the Amish/Mennonite Research Registry is completely voluntary. Whether or not you choose to allow your child to join this Research Registry will have no effect on your child's current or future medical care at the University of Pittsburgh Medical Center or other health care providers, and it will not affect your child's relationship with a health insurance provider or the University of Pittsburgh.

May I withdraw, at a future date, my consent for my child's participation in this Research Registry?

Your child may leave the Amish/Mennonite Research Registry at any time. To formally leave the Amish/Mennonite Research Registry, you should send a written and dated letter of your decision to have your child leave the Research Registry. The address can be found on the first page of this consent form.

VOLUNTARY CONSENT

All of the above has been explained to me and all of my current questions have been answered. I understand that I should ask questions about any part of my participation in the Amish Mennonite Research Registry at any time. Future questions will be answered by the coordinators of the registry. I understand that a copy of this consent form will be given to me.

I understand that any questions I have about my rights as a participant in the Research Registry will -be answered by the Human Subject Advocate of the IRB office, University of Pittsburgh (1-866-212-2668).

I understand that, as a minor (age less than 18 years), my child is not allowed to participate in this research study without my consent. Therefore, by signing this form, I give my consent for his/her participation in this research study.

By signing below, I agree to my child's participate in the Amish Mennonite Research Registry and provide my permission to share medical records with the research team.

_____

Printed Name of Child

_____ _____

Printed Name of Parent Relationship

_____ _____

Parent's Signature Date

VOLUNTARY ASSENT (12-17 YEAR OLDS ONLY)

Thank you for reading or listening about this study. Please think carefully about this study and decide if you want to be in it.

If you want to be in this study, you and your parents or guardian will need to sign these papers. If you sign this paper it means that you understand what will happen in the study. It also means that you want to be in this study and that you agree to do the things that are described in this paper. You will be given a copy of this paper to take home with you.

If you sign below, it means that you want to be in this study.

_____ _____

Signature of Child-Subject Date

_____ _____

Signature of Research Subject Date

VERFICATION OF EXPLANATION

I certify that I have carefully explained the purpose and nature of this research to (name of child) in age appropriate language. He/she has had an opportunity to discuss it with me in detail. I have answered all his/her questions and he/she provided affirmative agreement (i.e., assent) to participate in this research.

_____ _____

Signature of Person Obtaining Consent Date

CERTIFICATION OF INFORMED CONSENT

I certify that I have explained the nature and purpose of the Amish Mennonite Research Registry to the above-named individual, and I have discussed the possible risks and potential benefits of participation in this Research Registry. Any questions the individual has about this Research Registry have been answered, and the physicians and research staff associated with the Amish Mennonite Research Registry will be available to address future questions as they arise.

_____

Printed Name of Person Obtaining Consent

_____ _____

Signature of Person Obtaining Consent Date

CONSENT FOR CONTINUED PARTICIPATION

I am currently participating in a research study entitled “Amish Mennonite Research Registry”. Consent for my participation in this research study was initially obtained from my parents. I have now reached the age of 18 years and am able to provide direct consent for continued participation in this research study. I have had a chance to review the original consent document that my parents signed on my behalf and understand the research procedures that I am being asked to participate in during the remainder of the study.

I understand that I have the right to withdraw from the study at any time and that my decision to do so will not affect my care at the University of Pittsburgh Medical Center

The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations in the event that the research team is unavailable.

By signing this form, I agree to continue my participation in this research study.

_____ _____

Participant's Signature Date

Certification of Informed Consent

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions, concerns or complaints as they arise.

_____ _____

Printed Name of Person Obtaining Consent Role in Research Study

_____ _____

Signature of Person Obtaining Consent Date

APPENDIX C: LETTER OF SUPPORT FROM DR. HOLMES MORTON

D. Holmes Morton MD

May 9, 2016

University of Pittsburgh Institutional Review Board

3500 Fifth Avenue

Hieber Building, Suite 106

Pittsburgh, PA 15213

Dear IRB Committee:

I have been asked to write a letter of support for development of an Amish and Mennonite Community registry for Western Pennsylvania.

I have worked with the Lancaster County and now Mifflin County Plain Communities for over 30 years. Through early recognition of selected genetic disorders that were enriched by genetic-drift and population founder-effects, as well as through development of more timely interventions to manage disease, we at the Clinic for Special Children and the Central Pennsylvania Clinic have helped many individuals and families in the Plain Communities. We have been able to work within extended families to identify individuals in need of health care and have become an accepted healthcare resource. Community members have for over 50-years

participated in formal research about rare, inherited disorders. They often seek early diagnosis and help develop methods to improve outcomes.

Creating working relationships and disease catalogues is a slow process, usually by word-of-mouth among family, and Community, members. The Amish and Mennonite populations consist of many small subpopulations established by independent church groups. It is not possible to identify an individual, a Bishop or Deacon, who will provide "permission" to interact with the Community at large. Catalogues of disorders develop through information from the Pennsylvania Newborn Screening program, case studies, through family histories, and by reviews of medical-genetic literature, which is extensive for these well known populations. IRB oversight for reviews of case-records, natural history studies, observational reports about rare diseases, disease catalogues, as well as more formal research studies to develop new treatments have been overseen by multiple protocols approved by the IRB of Lancaster General Health.

The Registry envisioned by Drs. Gonzalez's and Vockley's proposal is designed to evolve in a similar manner. The investigators will reach out to Amish and Mennonite individuals in settings previously demonstrated as acceptable to the Plain Communities, including existing healthcare programs such as those offered through the Newborn Screening, Public Health, and clinical outreach in Mercer County by established healthcare providers in the Communities and UPMC-CHP specialty outreach clinics. Individuals may choose whether or not to participate in the registry through Informed Consents that explain the registry, the potential consequences of participation, and may include opportunities to electively take part in research. Medical care will be available regardless of the choice to take part, or not take part, in the registry.

Drs. Vockley and Gonzalez and their CHP-based clinicians and researchers have been respectful of the Amish and Mennonite Communities. I encourage you to approve their approach to out-reach to this Community to identify individuals and extended families who may benefit from better access to diagnosis, medical care, and to research that offers new hope for improved health outcomes within these underserved populations.

Sincerely,

D. Holmes Morton MD

Founding Pediatrician

Central Pennsylvania Clinic, A Medical Home for Special Children & Adults

PO Box 5806, 4527 East Main Street Suite E

Belleville PA 17004

Founding Pediatrician

Clinic for Special Children

PO Box 128, 535 Bunker Hill Road

Strasburg PA 17579

APPENDIX D: AMISH AND MENNONITE RESEARCH REGISTRY BROCHURE

Contact Us

If you have any questions about the Amish/Mennonite Research Registry, please do not hesitate to contact us!

Cate Walsh Vockley, MS, LCGC, Registry Coordinator
4401 Penn Avenue, Pittsburgh, PA 15224

Phone: 412-692-7349
Email: Catherine.walshvockley@chp.edu

Questions about your research participant rights?

Questions can be answered by the Human Subject Advocate of the IRB office, Univeristy of Pittsburgh (1-866-212-2668).

Children's Hospital of Pittsburgh

Children's Hospital of Pittsburgh UPMC
4401 Penn Avenue, Pittsburgh, PA 15224

What does it mean to participate in a registry?

AMISH MENNONITE RESEARCH REGISTRY

Amish Mennonite Registry

The purpose of this registry is to find members of the Plain Community who are interested in participating in future medical research studies. Having a registry makes it easier to contact and offer study participation to individuals who are appropriate for a new research study based on their own and their family medical history. Studies will focus on increasing knowledge about disorders affecting those who are Amish and Mennonite.

All Participation is

Voluntary and Confidential

The Benefits of Joining the Registry

The benefits of joining the Amish/Mennonite Research Registry include:

- Opportunities to participate in future research studies
- Research may have a positive impact on your medical care
- Research may have a positive impact on the general care in your community

If You Choose to Participate You Will be Asked to do the Following:

- Agree to allow access to your past, current, and future medical records
- Provide a detailed family health history
- Provide contact information that may be used to approach you about future research studies

Q&A

Who can participate in the Research Registry?

- Amish and Mennonite men and women age 18 or older
- Amish and Mennonite children with the permission of a parent

How is your privacy protected?

All data will be store in a password-protected database. Access to the database will be restricted to only registry staff.

Will it cost anything?

There will be no cost to you or your insurance provider.

Will you receive anything?

No, you will not receive any payment for your participation.

Is this voluntary?

Your participation is completely voluntary and your choice will not affect your current or future relationships with UPMC facilities or your insurance providers.

Can I withdraw in the future?

You may withdraw at any time from the registry with a written and dated notice to the principle investigator.

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